

IN THE UNITED STATES DISTRICT COURT  
FOR THE DISTRICT OF OREGON

CHRISTINA MCCLELLAN,

Plaintiff,

v.

I-FLOW CORPORATION, a Delaware corporation; DJO, L.L.C., a Delaware corporation; DJO INCORPORATED, a Delaware corporation; and PACIFIC MEDICAL, INC., a California corporation,

Defendants.

Civ. No. 07-1309-AA  
and related cases:

Civ. No. 07-1310-AA  
Civ. No. 07-1318-AA  
Civ. No. 07-1671-AA  
Civ. No. 08-0478-AA  
Civ. No. 08-0588-AA  
Civ. No. 08-1419-AA  
Civ. No. 09-0146-AA  
Civ. No. 09-0342-AA  
Civ. No. 09-0378-AA

OPINION AND ORDER

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AIKEN, Chief Judge:

In these related products liability actions, plaintiffs allege that they developed glenohumeral chondrolysis, the rapid and permanent loss of cartilage in the shoulder joint, after medical devices known as "pain pumps" were used to administer local anesthetics during and after arthroscopic surgery. Plaintiffs each seek non-economic damages of \$4,500,000 and economic damages ranging from \$1,050,000 to \$1,500,000 (or damages to be proven at trial), and against certain defendants,

punitive damages. Several plaintiffs also seek damages for loss of consortium.

Before the court are defendants' motions to exclude the general causation testimony of nine expert witnesses: Stephen Badylak, M.D.; Carl Basamania, M.D.; Charles Beck, M.D.; Jason Dragoo, M.D.; Sander Greenland, PhD; Frederick Matsen, M.D.; John Swanson, M.D.; Stephen Trippel, M.D.; and Martin Wells, PhD.<sup>1</sup> Defendants contend that the testimony of these experts is unreliable, irrelevant, and inadmissible under Federal Rule of Evidence 702 and Daubert v. Merrell Dow Pharm., Inc., 509 U.S. 579 (1993). Defendants also move to strike the testimony of Drs. Basamania and Matsen for failing to disclose information relevant to their expert opinions in violation of Federal Rule of Civil Procedure 26(a)(2)(B). Plaintiffs oppose the motions and, in turn, move to exclude the testimony of two defense expert witnesses, William Stetson, M.D. and Wayne Burkhead, Jr., M.D.

On November 17 and 18, 2009 and March 17, 2010 the court heard oral argument and brief testimony on the parties' motions after submission of extensive briefing. For the reasons set forth below, defendants' motions are granted with respect to the testimony of Frederick Matsen, M.D., Sander Greenland, PhD, and Martin Wells, PhD, granted in part with respect to Carl Basamania, M.D., and denied in all other respects. Plaintiffs' motions are denied.

### **BACKGROUND**

The glenohumeral joint is the ball-and-socket joint of the shoulder. A fibrous capsule encases the joint space, an area surrounding the joint that contains articular cartilage and synovial tissue. Articular cartilage is the thin layer of tissue that covers the ends of bones in the joint and

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<sup>1</sup>Defendants originally moved to strike the testimony of twelve expert witnesses. In response, plaintiffs clarified that three witnesses - Drs. Bowman, DiPaola, and Switlyk - intend to testify only as to specific causation.

provides a smooth, gliding surface to enable the bones to move. Unlike other types of tissue, articular cartilage has no nerves or blood supply and receives nutrients from synovial fluid within the joint space. Synovial tissue produces the synovial fluid which carries and diffuses nutrients into articular cartilage cells (chondrocytes) to continually renew the matrix of cartilage. In other words, synovial fluid is the "lifeblood" of articular cartilage. Trippel Expert Report, p. 4.

Glenohumeral chondrolysis is a very rare condition that results from the rapid and permanent destruction of articular cartilage in the shoulder joint. "Simply described, chondrolysis is the degeneration of cartilage cells, ending in cell death." D.J. Solomon et al., *Glenohumeral Chondrolysis After Arthroscopy: A Systematic Review of Potential Contributors and Causal Pathways*, 25 ARTHROSCOPY: J. ARTHROSCOPIC & RELATED SURG. 1329, 1330 (Nov. 2009). Cartilage cell death may occur from the inability of chondrocytes to maintain or produce cartilage matrix. Id. If not renewed, the cartilage matrix wears away with normal use of the joint until no protective tissue remains. The bones of the joint then rub against one another, causing debilitating pain and stiffness. Treatment options for chondrolysis are few, as shoulder joint replacement surgery has met with limited success. See J. Levy et al., *Young Patients with Shoulder Chondrolysis Following Arthroscopic Shoulder Surgery Treated with Total Shoulder Arthroplasty*, 17 J. SHOULDER ELBOW SURG. 380, 387 (May 2008) ("After nonoperative measures are exhausted, there are few options available for the patient who presents with chondrolysis after shoulder arthroscopy.").

Very few cases of chondrolysis were reported until the late 1990s when researchers described several patients who developed glenohumeral chondrolysis after receiving injections of gentian violet, a color contrast dye, during open surgery. See K. Tamai et al., *Chondrolysis of the Shoulder*

*Following a "Color Test"-Assisted Rotator Cuff Repair*, 68 ACTA ORTHOP. SCAND. 401 (Aug. 1997); Y. Nakagawa et al., *Glenohumeral Osteoarthritis Following a "Color Test" During Rotator Cuff Repair*, 57 BULL HOSP. JT. DIS. 216 (1998). Case reports during this time also identified a surgical irrigation solution and an acrylic bone cement as likely causes of cartilage destruction in the knee and hip joints. C. Douw et al., *Clinical and Pathological Changes in the Knee After Accidental Chlorhexidine Irrigation During Arthroscopy: Case Reports and Review of the Literature*, 80 J. BONE & JOINT SURG. 437 (May 1998); A. van Huyssteen & D. Bracey, *Chlorhexidine and Chondrolysis in the Knee*, 81 J. BONE & JOINT SURG. (U.K.) 995 (Nov. 1999); W. Leclair et al., *Rapid Chondrolysis After an Intra-Articular Leak of Bone Cement in Treatment of a Benign Acetabular Subchondral Cyst: An Unusual Complication of Percutaneous Injection of Acrylic Cement*, 29 SKELETAL RADIOL 275 (May 2000).

Still other cases of articular cartilage damage were reported after the use of radiofrequency devices (known as thermal devices or wands) and suture anchors during arthroscopic surgery. See R. Edwards et al., *Thermal Chondroplasty of Chondromalacic Human Cartilage*, 30 AM. J. SPORTS MED. 90 (Jan. 2002); W. Levine et al., *Chondrolysis Following Arthroscopic Thermal Capsulorrhaphy to Treat Shoulder Instability*, 87 J. BONE & JOINT SURG. 616 (Mar. 2005); see also G. Athwal et al., *Osteolysis and Arthropathy of the Shoulder After Use of Bioabsorbable Knotless Suture Anchors*, 88 J. BONE & JOINT SURG. 1840 (Aug. 2006); C. Good et al., *Glenohumeral Chondrolysis After Shoulder Arthroscopy with Thermal Capsulorrhaphy*, 23 ARTHROSCOPY 797 (July 2007); B. Coobs & R. LaPrade, *Severe Chondrolysis of the Glenohumeral Joint After Shoulder Thermal Capsulorrhaphy*, 38 AM J. ORTHOP. E34 (2009).

In 2004, surgeons reported three cases of glenohumeral chondrolysis in young athletes

following arthroscopic shoulder surgeries. Thermal devices were used during two of the surgeries, and one patient reportedly received a pain pump infused with bupivacaine and epinephrine, though the report is unclear whether the pain pump was placed intra-articularly. D. Petty et al., *Glenohumeral Chondrolysis After Shoulder Arthroscopy: Case Reports and Review of Literature*, 32 AM. J. SPORTS MED. 509, 511 (Mar. 2004). The authors suspected that thermal devices played a role in two of the three cases of chondrolysis but made no findings with respect to pain pump use. Id. at 514.

Beginning in 2003, Dr. Charles Beck, an orthopedic surgeon in Utah, observed that several of his patients developed chondrolysis after he performed arthroscopic surgeries and inserted pain pumps to administer bupivacaine and epinephrine directly into the shoulder joint. Dr. Beck eventually reviewed the medical records of patients involved in 152 shoulder arthroscopies and determined that chondrolysis developed in 12 of 19 (or 63%) of shoulders that received intra-articular continuous infusion of anesthetics via pain pump, while no cases of chondrolysis were reported in shoulders that were not treated with a pain pump.

In July 2005, Dr. Beck presented his findings to a group of orthopedic surgeons. He and a colleague, Dr. Brent Hansen, wrote a paper analyzing his research, and in July 2007 their paper was published in the *American Journal of Sports Medicine*. See B. Hansen & C. Beck, *Postarthroscopic Glenohumeral Chondrolysis*, 35 AM. J. SPORTS MED. 1628 (July 2007) [hereinafter Hansen/Beck Study]. Physicians and researchers have published additional reports of glenohumeral chondrolysis after arthroscopic surgery and discussed potential causes of the disease, including the use of pain pumps for continuous infusion of local anesthetics. See, e.g., P. Greis et al., *Bilateral Shoulder Chondrolysis Following Arthroscopy*, 90 J. BONE & JOINT SURG. 1338 (June 2008); S. Anderson et

al., *Chondrolysis of the Glenohumeral Joint - Abstract*, 24 J. ARTHROSCOPY SUPP. e13 (Apr. 2008); A. McNickle et al., *Postsurgical Glenohumeral Arthritis in Young Adults*, \_\_ AM. J. SPORTS MED. \_\_ (June 2009); M. Saltzman et al., *Postsurgical Chondrolysis of the Shoulder*, 32 ORTHOPEDICS 215 (June 2009); D. Bailie & T. Ellenbecker, *Severe Chondrolysis After Shoulder Arthroscopy: A Case Series*, \_\_ J. SHOULDER ELBOW SURG. \_\_ (Jan. 2009).

Further, researchers have conducted in vitro and animal studies on the chondrotoxicity of local anesthetics. N. Dogan et al., *The Effects of Bupivacaine and Neostigmine on Articular Cartilage and Synovium in the Rabbit Knee Joint*, 32 J. INT'L MED. RES. 513 (Sept. 2004); C. Chu et al., *In Vitro Exposure to 0.5% Bupivacaine is Cytotoxic to Bovine Articular Chondrocytes*, 22 ARTHROSCOPY 693 (July 2006) [Chu I]; A. Gomoll et al., *Chondrolysis After Continuous Intra-Articular Bupivacaine Infusion*, 22 ARTHROSCOPY 813 (Aug. 2006) [Gomoll I]; J. Karpie & C. Chu, *Lidocaine Exhibits Dose- and Time-Dependent Cytotoxic Effects on Bovine Articular Chondrocytes In Vitro*, 35 AM. J. SPORTS MED. 1621 (Oct. 2007); S. Piper & H. Kim, *Comparison of Ropivacaine and Bupivacaine Toxicity in Human Articular Chondrocytes*, 90 J. BONE & JOINT SURG. 986 (May 2008); Chu et al., *The In Vitro Effects of Bupivacaine on Articular Chondrocytes*, 90 J. BONE & JOINT SURG. 814 (U.K.) (June 2008) [Chu II]; J. Dragoo et al., *The Effect of Local Anesthetics Administered Via Pain Pump on Chondrocyte Viability*, 36 AM. J. SPORTS MED. 1484 (Aug. 2008); Gomoll et al., *Long-Term Effects of Bupivacaine on Cartilage in a Rabbit Shoulder Model*, 37 AM. J. SPORTS MED. 72, 75-76 (Jan. 2009) [Gomoll II]; Lo et al., *Local Anesthetics Induce Chondrocyte Death in Bovine Articular Cartilage Disks in a Dose- and Duration-Dependent Manner*, 25 ARTHROSCOPY: J. ARTHROSCOPIC & RELATED SURG. 707 (July 2009).

Finally, authors have published reviews of the relevant medical literature. B. Busfield & D.

Romero, *Pain Pump Use After Shoulder Arthroscopy as a Cause of Glenohumeral Chondrolysis*, 25 ARTHROSCOPY 647 (Jan. 2009); E. Fester & F. Noyes, *Postoperative Chondrolysis of the Knee: 3 Case Reports and Review of the Literature*, \_\_ AM. J. SPORTS MED. 1 (July 2009); R. Kang et al., *Complications Associated with Anterior Shoulder Instability Repair*, 25 ARTHROSCOPY 909 (Aug. 2009).

In November 2009, the Food and Drug Administration (FDA) issued a bulletin entitled "Information for Healthcare Professionals - Chondrolysis Reported with Continuously Infused Local Anesthetics." Horwitz Decl. in Supp. Defs.' Suppl. Mem., Ex. H (updated Feb.16, 2010). The bulletin states that upon reviewing 35 reports of chondrolysis, "[t]he significance of this injury to otherwise healthy young adults warrants notification to health care professionals . . . to follow the instructions for use of elastomeric infusion devices, and to not use these devices for continuous intra-articular infusion of local anesthetics after orthopedic surgery." Id. Ex. H, p. 1. The FDA made clear that "[n]either local anesthetics nor infusion devices are approved for an indication of continuous intra-articular infusion." Id. The FDA further announced that it "is requiring the drug manufacturers to update their product labels to warn healthcare professionals about this potential serious adverse effect" and "is also exploring possible options for addressing the safety issues with the infusion devices (e.g., labeling changes, etc.)." Id.

On August 31, 2007, the first pain pump products liability action was filed in this district, and 23 cases are now pending before the court. Plaintiffs allege that the intra-articular use of pain pumps to administer a continuous infusion of local anesthetics [hereinafter referred to as "continuous infusion"] either caused or substantially contributed to their development of glenohumeral chondrolysis. Plaintiffs bring suit against the manufacturers and distributors of the accused pain

pumps, including Stryker Corp., Stryker Sales Co., McKinley Medical L.L.C., DJO, L.L.C., I-Flow Corp., and Pacific Medical, Inc. Plaintiffs allege claims of defective design and labeling, failure to warn, and negligence based on defendants' failure to warn physicians of the risks associated with the intra-articular use of pain pumps and defendants' manufacture and promotion of pain pumps for intra-articular uses that were not approved by the FDA.<sup>2</sup>

The parties agree that plaintiffs must present evidence of both general and specific causation to prevail on their claims. "General causation is established by demonstrating, often through a review of scientific and medical literature, that exposure to a substance *can cause* a particular disease[.]" while specific causation "is established by demonstrating that a given exposure *is the cause* of an individual's disease[.]" REFERENCE MANUAL ON SCIENTIFIC EVIDENCE, 444 (Fed. Judicial Ctr. 2d ed. 2000) [REFERENCE MANUAL] (emphasis added); see also Golden v. CH2M Hill Hanford Group, Inc., 528 F.3d 681, 683 (9th Cir. 2008). Thus, plaintiffs must present expert testimony to show by a preponderance of the evidence that continuous infusion can and did cause plaintiffs' chondrolysis. See Joshi v. Providence Health Sys. of Oregon Corp., 198 Or. App. 535, 536-37, 108 P.3d 1195 (2005) (when causation involves a complex medical question, Oregon law requires expert testimony establishing "a reasonable medical probability" of causation). Per the parties' agreement, the instant motions are limited to whether plaintiffs' experts offer reliable testimony on general causation.

### APPLICABLE LAW

Federal Rule of Evidence 702 (Rule 702) governs the admissibility of expert testimony. Rule

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<sup>2</sup>Several plaintiffs also allege shareholder liability claims against DJO, Inc., a parent corporation of DJO, L.L.C.



702 permits a qualified expert to present testimony that "will assist the trier of fact" in understanding the evidence or in determining a factual issue, so long as "(1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case." Fed. R. Evid. 702; see also Daubert, 509 U.S. at 593-95. "In short, an expert's conclusion must meet the 'trilogy of restrictions on expert testimony: qualification, reliability and fit.'" In re Human Tissue Prods. Liab. Litig., 582 F. Supp. 2d 644, 655 (D.N.J. 2008) (quoting Schneider v. Fried, 320 F.3d 396, 404 (3d Cir. 2003)). The proponent of the evidence must prove its admissibility by a preponderance of the evidence. Daubert, 509 U.S. at 592 n.10.

Rule 702 codifies the reliability requirements set forth in *Daubert* and subsequent Supreme Court decisions. See Kumho Tire Co. v. Carmichael, 526 U.S. 137 (1999); Gen. Elec. Co. v. Joiner, 522 U.S. 136 (1997). Prior to *Daubert*, the admissibility of expert testimony was governed by "the traditional 'general acceptance' test enunciated in *Frye v. United States*, which required that a scientific technique be generally accepted in the relevant scientific community to be admissible." In re Fosamax Prods. Liab. Litig., 645 F. Supp. 2d 164, 172 (S.D.N.Y. 2009). In finding the *Frye* test superceded by the Federal Rules of Evidence, the Supreme Court in *Daubert* explained that "a rigid general acceptance requirement would be at odds with the liberal thrust of the Federal Rules and their general approach of relaxing the traditional barriers to opinion testimony." Daubert, 509 U.S. at 588 (quotation marks and citations omitted). At the same time, the Supreme Court recognized the limits of "purportedly scientific evidence." Id. at 589.

Under *Daubert*, the trial judge bears the responsibility of "gatekeeper" to ensure "that an expert's testimony both rests on a reliable foundation and is relevant to the task at hand." Daubert,

509 U.S. at 597. This inquiry requires "a preliminary assessment of whether the reasoning or methodology underlying the testimony is scientifically valid and of whether that reasoning or methodology properly can be applied to the facts in issue." *Id.* at 592-93. "Pertinent evidence based on scientifically valid principles will satisfy those demands." *Id.* at 597.

Reliable testimony must be grounded "in the methods and procedures of science," and signify knowledge beyond "subjective belief or unsupported speculation." *Daubert*, 509 U.S. at 590. Generally, the court's analysis focuses on the methodology underlying an expert's testimony rather than the expert's ultimate conclusions. *Daubert*, 509 U.S. at 595. At the same time, "conclusions and methodology are not entirely distinct from one another," and "[a] court may conclude that there is simply too great an analytical gap between the data and the opinion proffered." *Joiner*, 522 U.S. at 146.

*Daubert* identifies four factors that the court may consider in assessing reliability, including: 1) whether a theory or technique can be and has been tested; 2) whether a theory has been subjected to peer review and publication; 3) whether a "particular scientific technique" has a known or potential rate of error; 4) and whether the theory or technique enjoys general acceptance within the "relevant scientific community." *Daubert*, 509 U.S. at 593-94. However, "*Daubert* makes clear that the factors it mentions do *not* constitute a 'definitive checklist or test.'" *Kumho*, 526 U.S. at 150 (quoting *Daubert*, 509 U.S. at 593). Rather, these factors "may or may not be pertinent in assessing reliability, depending on the nature of the issue, and expert's particular expertise," and the subject matter of the proffered testimony. *Id.* (citation omitted).

Relevant expert testimony "logically advances a material aspect of the proposing party's case." *Daubert v. Merrell Dow Pharm., Inc.*, 43 F.3d 1311, 1315 (9th Cir. 1995) (*Daubert II*). An

expert's testimony must assist the trier of fact and relate to, or "fit," the underlying facts of the case. Id. at 591.

Though the court must ensure that an expert's opinion is supported by sufficient data and reliable methodology, the inquiry is "a flexible one," depending on "the particular circumstances of the particular case at issue." Kumho, 526 U.S. at 150. In other words, an expert's testimony must rest on "good grounds, based on what is known." Daubert, 509 U.S. at 590. Ultimately, the court must ensure that an expert "employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field," Kumho, 526 U.S. at 152, such that the expert's "work product amounts to 'good science.'" Daubert II, 43 F.3d at 1315 (quoting Daubert, 509 U.S. at 593).

### **DISCUSSION**

At first glance, the reliability of plaintiffs' experts' testimony seems fairly straightforward. Plaintiffs' experts opine that, to a reasonable degree of medical probability, continuous infusion can cause chondrolysis. Eminently qualified, plaintiffs' experts base their opinions on their knowledge and experience, in vitro (laboratory) and animal studies demonstrating the chondrotoxicity of local anesthetics typically used with continuous infusion, case reports associating continuous infusion with chondrolysis, and the temporal relationship between the use of continuous infusion and the increased and unprecedented reports of chondrolysis.

Yet, defendants assert numerous challenges against the admission of plaintiffs' expert testimony. Defendants argue that medical science lacks sufficient facts or data regarding the cause of chondrolysis, and no conclusive evidence, such as epidemiological studies, establishes a causal link. Absent such evidence, defendants maintain that plaintiffs' opinions are unreliable products of

litigation research that lack peer review, general acceptance in the profession, or any hallmark of scientific validity. Given their broad application, I address these arguments before discussing the opinions of individual experts.

#### A. Certainty of Evidence Supporting General Causation

Defendants argue that plaintiffs' experts erroneously and unreliably "rule in" continuous infusion as a cause of chondrolysis, despite the prevalence of uncertain and inconclusive data. In support of their argument, defendants cite several chondrolysis studies, including Dr. Beck's, which submit that the exact cause of chondrolysis and its biological mechanism is "unclear," "unknown," "speculative," "multifactorial," and requires "further study." Hansen, p. 1628; Bailie, p. 2; Greis, p. 1338; Busfield, p. 651; Levy, p. 384; Gomoll I, p. 814, Solomon, pp. 1339-41; see also Basamania Dep., Aug. 15, 2009, p. 410-11 ("[T]he best we can say at this point in time is that it appears multifactorial. It could be a dilution, it could be pH, it could be inhibition of the synovial cells to produce more fluids.").

While defendants concede that some of the medical literature supports an association between continuous infusion and chondrolysis, they maintain that association is distinct from and cannot reliably support causation. See Siharath v. Sandoz Pharm. Corp., 131 F. Supp. 2d 1347, 1372 (N.D. Ga. 2001) ("Doctors in their day-to-day practices stumble upon coincidental occurrences and random events and often follow human nature, which is to confuse association and causation."). Absent conclusive evidence of causation, defendants insist that plaintiffs' experts' opinions are unreliable "'leaps of faith' unsupported by good science." Kilpatrick v. Breg, Inc., 2009 WL 2058384, at \*3 (S.D. Fla. June 25, 2009) (quoting Rider v. Sandoz Pharm., 295 F.3d 1194, 1202 (11th Cir. 2002)).

Defendants' mantra of conclusive causal evidence repeats throughout their various arguments. Whether challenging the scientific validity of expert methodologies, the general acceptance of expert opinion, or the influence of litigation, defendants repeatedly and consistently revert to what is the essence of their *Daubert* motions: plaintiffs' experts cannot testify that continuous infusion causes glenohumeral chondrolysis because no medical or epidemiological study conclusively says it does. Taking defendants' argument to its logical conclusion, defendants would have plaintiffs prove causation to a medical certainty before expert testimony could be admitted. I find defendants' argument wholly inconsistent with *Daubert* and the fundamental premise of Rule 702.

Rule 702 permits expert testimony that is helpful to the trier of fact, reliable, and relevant. To that end, *Daubert* was intended to exclude "junk science" - unsupported testimony or evidence cloaked in the credentials of a testifying expert - that would confuse or mislead rather than "assist the trier of fact." Best v. Lowe's Home Ctrs., Inc., 563 F.3d 171, 176-77 (6th Cir. 2009) ("*Daubert* attempts to strike a balance between a liberal admissibility standard for relevant evidence on the one hand and the need to exclude misleading 'junk science' on the other."). *Daubert* did not, however, impose an "exacting standard of causality" beyond the preponderance of the evidence "simply because scientific issues are involved." In re Ephedra Prods. Liab. Litig., 393 F. Supp. 2d 181, 190 (S.D.N.Y. 2005). "It would be unreasonable to conclude that the subject of scientific testimony must be 'known' to a certainty; arguably, there are no certainties in science." Daubert, 509 U.S. at 590; see also Basamania Dep. Aug. 15, 2009, p. 435 ("There's [sic] very few things in medic[ine] where it's absolutely established that X [causes] Y."). Moreover, "[l]ack of certainty is not, for a qualified expert, the same thing as guesswork." Primiano v. Cook, \_\_\_ F.3d \_\_\_, 2010 WL 1660303, at \*5 (9th

Cir. Apr. 27, 2010).<sup>3</sup>

Consequently, the proper focus under *Daubert* is whether an expert's testimony rests on evidence reliably derived from scientific methodology and is relevant to the facts of the case, not whether plaintiffs' experts can *prove* the point of their testimony. Ambrosini v. Labarraque, 101 F.3d 129, 135 (D.C. Cir. 1996) ("The dispositive question is whether the testimony will 'assist the trier of fact to understand the evidence or to determine a fact in issue,' not whether the testimony satisfies the plaintiff's burden on the ultimate issue at trial.") (citation omitted). Indeed, establishing reliability should not mean that plaintiffs "have to prove their case twice - they do not have to demonstrate to the judge by a preponderance of the evidence that the assessments of their experts are *correct*, they only have to demonstrate by a preponderance of evidence that their opinions are *reliable*." In re Paoli R.R. Yard PCB Litig., 35 F.3d 717, 744 (3d Cir. 1994); Allison v. McGhan Med. Corp., 184 F.3d 1300, 1312 (11th Cir. 1999) (accord); In re Ephedra, 393 F. Supp. 2d at 193 ("*Daubert's* dictum about scientific validity" is not "authority for increasing the burden of proof imposed by substantive law"). Reliability under *Daubert* does not depend on "the correctness of the expert's conclusions but [on] the soundness" of the methodology. Daubert II, 43 F.3d at 1318.

Thus, even if the medical evidence asserts "only" an association between continuous infusion and chondrolysis, plaintiffs' experts' testimony should not be excluded if they adequately explain why the association is valid and how causation can be inferred from it. Kennedy v. Collagen Corp., 161

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<sup>3</sup>At oral argument on March 17, 2010, defense counsel hastened to inform the court that *Primiano* did not involve the issue of general causation, and reliance on its analysis would improperly conflate distinct areas of *Daubert* jurisprudence. While I am well aware of the factual distinctions between these cases and *Primiano*, the Ninth Circuit's analysis of physician expert testimony under *Daubert* has broad application and is not limited to claims similar to that brought in *Primiano*.

F.3d 1226, 1229-30 (9th Cir. 1998); see also United States v. W.R. Grace, 504 F.3d 745, 766 (9th Cir. 2007); Heller v. Shaw Indus., Inc., 167 F.3d 146, 154-55 (3d Cir. 1999); In re Ephedra, 393 F. Supp. 2d at 190 (Rule 702 is one of threshold admissibility and does not preclude evidence of a kind typically relied on by experts in the relevant field). "A trial court should admit medical expert testimony if physicians would accept it as useful and reliable, but it need not be conclusive because medical knowledge is often uncertain." Primiano, 2010 WL 1660303, at \*5 (quotation marks and citation omitted). This is particularly true where plaintiffs' experts need only testify to a medically reasonable *probability* of causation between continuous infusion and chondrolysis. Baughman v. Pina, 200 Or. App. 15, 18, 113 P.3d 459 (2005).

Defendants nonetheless argue that plaintiffs' experts cannot "rule in" continuous infusion as a cause of chondrolysis through the differential diagnosis methodology without conclusive evidence of causation. Defendants maintain that a differential diagnosis typically "rules out" suspected causes to establish specific causation, but only after the accused product or agent has been "ruled in" as a causative factor. See Ruggiero v. Warner-Lambert Co., 424 F.3d 249, 254 (2d Cir. 2005); see, e.g., Norris v. Baxter Healthcare Corp., 397 F.3d 878, 885 (10th Cir. 2005); In re Rezulin Prods. Liab. Litig., 2004 WL 2884327, at \*4 (S.D.N.Y. Dec. 10, 2004); Hall v. Baxter Healthcare Corp., 947 F. Supp. 1387, 1413 (D. Or. 1996). Thus, because continuous infusion has not been proven as a cause of chondrolysis, defendants argue that differential diagnosis is not reliable to establish general causation. I disagree.

"Differential diagnosis, or differential etiology, is a standard scientific technique of identifying the cause of a medical problem by eliminating the likely causes until the most probable one is isolated." Westberry v. Gislaved Gummi AB, 178 F.3d 257, 262 (4th Cir. 1999); REFERENCE

MANUAL, p. 443.<sup>4</sup> Here, several of plaintiffs' experts applied differential diagnosis in developing their opinions that continuous infusion can cause chondrolysis. See Badylak Expert Report, p. 3; Beck Expert Report, pp. 13-15; Swanson Expert Report, p. 4; Trippel Expert Report, p. 14; Beck *Grossnickle* testimony, Mar. 3, 2009, Vol. 5A, p. 1107 ("I believe there's an association with this same condition because I can't find any other reason for it."); Basamania Dep. Aug. 15, 2009, p. 428 ("[C]hondrolysis was an exceedingly rare occurrence until the introduction of these [pain pumps].").

Several courts agree that the differential diagnosis methodology "does not (necessarily) support an opinion on general causation, because, like any process of elimination, it assumes that the final, suspected 'cause' remaining after this process of elimination must actually *be capable* of causing the injury." See Ruggiero, 424 F.3d at 254 (quotation marks and citation omitted); Henricksen v. ConocoPhillips Co., 605 F. Supp. 2d 1142, 1158 (E.D. Wash. 2009) ("[D]ifferential diagnosis cannot demonstrate general causation, because it assumes, without proving, that all of the potential causes considered are capable of causing the condition at issue."); Hall, 947 F. Supp. at 1413 ("Indeed, differential diagnosis *assumes* that general causation has been proven for the list of possible causes it eliminates[.]").

At the same time, "[t]here may be instances where, because of the rigor of differential diagnosis performed, the expert's training and experience, the type of illness or injury at issue, or some other case-specific circumstance, a differential diagnosis is sufficient to support an expert's

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<sup>4</sup>Physicians typically use the term "differential diagnosis" to "describe the process of determining which of several *diseases* is causing the patient's *symptoms*," while expert witnesses use the term "differential diagnosis" or "differential etiology" to describe the process of determining and identifying the cause of a patient's condition, often by eliminating or "ruling" out other causes. REFERENCE MANUAL, pp. 444, 470 n.112. For purposes of consistency and clarity, I adopt the latter meaning of "differential diagnosis" as the process of determining cause.



opinion in support of both general and specific causation." Ruggiero, 424 F.3d at 254. I find this to be one of those instances.

Unlike the majority of cases in which differential diagnosis was held insufficient to rule in a potential causative factor, plaintiffs here do not allege toxic exposure through air, water, or groundwater contamination, or through the ingestion of a pharmaceutical drug. See, e.g., Ruggiero, 424 F.3d at 251; Henricksen, 605 F. Supp. 2d at 1148-49; Bickel v. Pfizer, 431 F. Supp. 2d 918, 923-24 (N.D. Ind. 2006); In re Rezulin Prods. Liab. Litig., 369 F. Supp. 2d 398, 436-37 (S.D.N.Y. 2005); Siharath, 131 F. Supp. 2d 1349-50; Cavallo v. Star Enter., 892 F. Supp. 756, 771 (E.D. Va. 1995). Nor do plaintiffs allege that exposure to toxins, medications, or medical products caused cancer, stroke, birth defects, or other systemic disease or injury unrelated to the area or purpose of exposure. See, e.g., Hollander v. Sandoz Pharm. Corp., 289 F.3d 1193, 1210-11 (10th Cir. 2002); Raynor v. Merrell Pharm. Inc., 104 F.3d 1371, 1375-76 (D.C. Cir. 1997); Doe v. Ortho-Clinical Diagnostics, Inc., 440 F. Supp. 2d 465, 476-77 (M.D.N.C. 2006); Glastetter v. Novartis Pharm. Corp., 107 F. Supp.2d 1015, 1027-28 (E.D. Mo. 2000); In re Breast Implant Litig., 11 F. Supp. 2d 1217, 1229-30 (D. Colo. 1998); Hall, 947 F. Supp. at 1412. In such cases, a whole host of potential causal factors - medical, environmental, occupational - may be implicated, such that the connection between the accused product and resulting injury is not readily apparent, if not tenuous. Depending on the specific facts of alleged injury and the relevant evidence cited to support causation, the differential diagnosis methodology might well be inappropriate and insufficient to reach *Daubert's* reliability threshold for general causation. In other words, "the basis for establishing the scientific validity of a differential diagnosis will vary depending on the type of injury" and whether it involves a "complicated biological explanation," "a long latency period," or "the lack of a single sharp exposure

event." Marcum v. Adventist Health System/West, 345 Or. 237, 249, 193 P.3d 1 (Or. 2008) (en banc) (citation omitted); see also Heller, 167 F.3d at 154 (the "overall determination" of whether an expert opinion is based on "good grounds" will depend on the strength of case-specific factors such as temporal relationship); In re Ephedra Prods. Liab. Litig., 478 F. Supp. 2d 624, 633 (S.D.N.Y. 2007).

In contrast, plaintiffs allege the localized injury of glenohumeral chondrolysis after anesthetics were continuously and directly infused into their shoulder joints - a part of the human body that is encased and has no blood supply. Further, plaintiffs and other patients developed chondrolysis within a relatively short time after arthroscopies with continuous infusion, and reports of chondrolysis increased dramatically after physicians began administering local anesthetics via pain pumps. Thus, not only does a direct physical correlation exist between the point of exposure and the resulting injury to the shoulder joint, there is an appreciable temporal relationship between the exposure to continuous infusion and the development of chondrolysis. See Best, 563 F.3d at 180-81 (finding differential diagnosis admissible regarding cause of loss of smell because of temporal proximity to chemical exposure and evidence that accused chemical caused mucous membrane irritation); Westberry, 178 F.3d at 262 (admitting expert testimony based on differential diagnosis despite lack of "studies showing that talc, at any threshold level, causes sinus disease"); Perkins v. Origins Medsystems, Inc., 299 F. Supp. 2d 45, 58-61 (D. Conn. 2004) (finding differential diagnosis reliable for purposes of establishing general causation where plaintiff alleged pain and injury from placement of surgical tacks).

In fact, numerous courts have approved opinions based on differential diagnosis to show general causation, despite the absence of conclusive causal evidence. See Clausen v. M/V New

Carissa, 339 F.3d 1049, 1058-59 (9th Cir. 2003); Mattis v. Carlon Elec. Prods., 295 F.3d 856, 861 (8th Cir. 2002). Turner v. Iowa Fire Equip. Co., 229 F.3d 1202, 1208-09 (8th Cir. 2000) (approving differential diagnosis for general causation but finding testimony inadmissible on other grounds); see also Heller, 167 F.3d at 154; Kennedy, 161 F.3d at 1229-30; Zuchowicz v. United States, 140 F.3d 381, 387 (2d Cir. 1998); Benedi v. McNeil-P.P.C., Inc., 66 F.3d 1378, 1384 (4th Cir. 1995); McCulloch v. H.B. Fuller Co., 61 F.3d 1038, 1043-44 (2d Cir. 1995); In re Paoli, 35 F.3d at 744; In re Fosamax, 645 F. Supp. 2d at 178-79 (a physician need not rely on controlled studies to "rule in" a suspected cause); Yarchak v. Trek Bicycle Corp., 208 F. Supp. 2d 470, 499 (D.N.J. 2002) (expert testimony on general causation should be admitted when based on a "thorough differential diagnosis [that] reliably flows from the underlying facts of the case").

For example, in *Kennedy*, the plaintiff's expert Dr. Spindler opined that Zyderm, a collagen product comprised of bovine tissues injected under the skin for a "smoother appearance," could cause the autoimmune disorder of atypical systemic lupus erythematosus (SLE). 161 F.3d at 1228. Dr. Spindler's proffered expert testimony was "based on his knowledge of the connection between collagen and various autoimmune disorders, combined with his observation of [the plaintiff]'s injuries and her medical history and laboratory tests." *Id.* at 1229-30. The district court excluded Dr. Spindler's testimony, focusing "on the lack of specific studies proving Zyderm causes lupus, and the absence of consensus in the medical community on this point." *Id.* at 1230.

The Ninth Circuit reversed, finding that "the district court ignored the scientific studies relied upon by Dr. Spindler that reinforce the validity of the *methodology* Dr. Spindler relied upon in reaching his conclusion." *Id.* In particular, the court noted that Dr. Spindler relied on peer-reviewed studies establishing "that Zyderm induces the body to produce the same autoimmune antibodies that

are the hallmark of autoimmune diseases like SLE." Kennedy, 161 F.3d at 1228.<sup>5</sup> While recognizing that Dr. Spindler's opinion could be viewed with skepticism, the court nonetheless found Dr. Spindler's methodology reliable:

*The fact that a cause-effect relationship between Zyderm and lupus in particular has not been conclusively established does not render Dr. Spindler's testimony inadmissible. . . . Dr. Spindler's analogical reasoning was based on objective, verifiable evidence and scientific methodology of the kind traditionally used by rheumatologists. This is precisely what Daubert requires.*

Id. at 1230 (citations omitted) (emphasis added). Although the Ninth Circuit did not employ the terms "differential diagnosis" or "general causation," such was the methodology employed by Dr. Spindler in asserting a general causation opinion. Id. at 1228 ("Dr. Spindler relied upon a wide variety of objective, verifiable evidence in forming his opinion that Zyderm causes autoimmune disorders such as atypical SLE."); see also Clausen, 339 F.3d at 1058-60 (holding that "a lack of specific scholarly support" did not prevent the admission of differential diagnosis testimony ruling in oil toxicity as cause of oyster morbidity, where the expert relied on field studies, laboratory studies, history of the oyster site, findings of oil contamination, and the temporal relationship between the oil spill and oyster morbidity).<sup>6</sup>

Similar to the facts in *Kennedy*, plaintiffs' experts here rely on "objective, verifiable evidence" of in vitro and animal studies demonstrating the chondrotoxicity of local anesthetics, case

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<sup>5</sup>Dr. Spindler also relied on clinical trials, product studies conducted by the defendant, and an investigation by the State of Texas Department of Health. Id. at 1228.

<sup>6</sup>Defendants emphasize that the defense expert in *Clausen* agreed that oil toxicity could cause oyster morbidity, while no defense expert here agrees that continuous infusion can cause chondrolysis. Regardless, the experts in *Clausen* disagreed as to the level of oil that could cause toxicity and the defendants strenuously argued that it was error to "rule in" low-level oil toxicity as a cause of oyster morbidity.

series describing an association between continuous infusion and chondrolysis, the temporal relationship between continuous infusion and chondrolysis, and reports of continuous infusion as an isolated or common factor.<sup>7</sup> Cf. Joiner, 522 U.S. at 145-46 (medical evidence relied on was "far removed," suggested "no link" between exposure and injury, and provided "no grounds for associating" exposure and injury). Given these facts, I find that plaintiffs' experts need not present conclusive evidence of causation, and that they offer "independently reliable evidence" to rule in continuous infusion as a cause of chondrolysis. Hollander, 289 F.3d at 1210 (citing Zuchowicz, 140 F.3d at 385-87 and Kennedy, 161 F.3d at 1228-30); In re Ephedra, 393 F. Supp. 2d at 187-88 (discussing Zuchowicz and McCulloch generally).<sup>8</sup>

Finally, I remain unpersuaded by defendants' reliance on *Kilpatrick*. There, the district court excluded an expert's proffered testimony that continuous infusion can cause chondrolysis, because no evidence cited by the expert "proved" causation. Kilpatrick 2009 WL 2058384, at \*7-9. In

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<sup>7</sup>I note that, notwithstanding the lack of conclusive evidence, defense expert Dr. Burkhead considers thermal energy and a patient's age as potential causes of chondrolysis, because each has "been reported as an isolated factor." See Burkhead Dep., Aug. 31, 2009, pp. 30, 34, 35. Dr. Burkhead explained: "So, again, when I look at - use the term causative, if it's something that's isolated usage where you can't see anything else that might have caused it, then I think it's reasonable to use that terminology." Id. at 48; see also Greis, p. 1344 (finding continuous infusion to be a "probable causative factor" because "other causes did not seem to play a role").

<sup>8</sup>Defendants also argue that plaintiffs' experts must rely on epidemiological data showing that continuous infusion doubles the risk of developing chondrolysis. However, "the 'doubling of the risk' is a measure courts use to determine whether a substance is capable of causing harm in the absence of any evidence other than epidemiological evidence of toxicity." In re Berg Litig., 293 F.3d 1127, 1130 (9th Cir. 2002). Here, plaintiffs' alleged injury renders these cases distinguishable from those requiring such data, and plaintiffs do not rely solely on epidemiological studies. See id. (alleging mass exposure to radiation caused cancer); Daubert II, 43 F.3d at 1320-21 (alleging ingestion of Bendectin caused birth defects) Hall, 947 F. Supp. at 1402-03 (alleging silicone leakage from breast implants caused systemic illness of atypical connective tissue disease).

particular, the district court found that the "unsettled" state of the medical literature - the Hansen/Beck Study, the Greis case series, and Gomoll I - was insufficient to establish causation. Id. Further, the district court found that the expert's reliance on patient records and the medical literature had no "known rate of error." Id. at \*7-9.

The court even went so far as to criticize the expert's failure to account for the 7 of 19 shoulders in the Hansen/Beck Study that received continuous infusion but did not develop chondrolysis, characterizing the expert's lack of explanation as "an unexplained 40% error rate." Id. at \*5. If 100% of patients receiving continuous infusion must develop chondrolysis before an expert may reliably opine on causation, expert testimony would hardly be necessary. Given that the court did not cite statistical or epidemiological evidence in assessing a "40% error rate," one can only surmise that it was the court's own finding, one made without evidentiary support. However, Rule 702 imposes on the court neither "the obligation" nor "the authority to become [an] amateur scientist[] in order to perform" its gatekeeping role. See Daubert, 509 U.S. at 600-01 (Rehnquist, C.J., concurring in part).

I find that the district court in *Kilpatrick* went far beyond its gatekeeping function and "failed to distinguish between the threshold question of admissibility of expert testimony and the persuasive weight to be accorded such testimony by a jury." Kennedy, 161 F.3d at 1228. Importantly, it is not the court's role to decide whether the proffered expert testimony sufficiently proves that continuous infusion can cause chondrolysis; rather, it is the court's duty to ensure that the proffered expert testimony is sufficiently reliable to be admitted at trial for consideration by the trier of fact. "Under *Daubert*, the district judge is 'a gatekeeper, not a fact finder.'" Primiano, 2010 WL 1660303, at \*4 (quoting United States v. Sandoval-Mendoza, 472 F.3d 645, 654 (9th Cir. 2006)).

In keeping with the court's proper role and the "liberal thrust" of Rule 702, I will not exclude plaintiffs' expert testimony simply because the evidence supporting it does not establish causation to a scientific or medical certainty. Daubert, 509 U.S. at 588.

#### B. Sufficiency of Facts and Data Supporting General Causation

Defendants punctuate the lack of epidemiological studies on chondrolysis and maintain that plaintiffs' experts impermissibly extrapolate causal connections from in vitro studies, animal studies, and case series, such that the "analytical gap" between the medical evidence and their opinions grows too wide to meet the reliability threshold of Rule 702. Defendants further argue that plaintiffs' experts unsuccessfully attempt to fill the "gaps" between the medical evidence and their opinions through generalized references to the whole of medical evidence.

##### 1. Epidemiological Evidence

Plaintiffs' experts do not cite an epidemiological study in support of their general causation opinions, to defendants, a "fatal evidentiary flaw" that precludes expert testimony on general causation. Defendants argue that without a prospective, controlled epidemiological study to establish the background rate and relative risk of chondrolysis in the general population, plaintiffs' experts' opinions are merely "untested hypothes[es]" unsupported by "good science." Hall, 947 F. Supp. at 1401-02. Plaintiffs respond that epidemiological evidence is not necessary to support their claims. Nonetheless, plaintiffs contend that statistical analysis of the Hansen/Beck Study provides sufficient epidemiological evidence of the background rate and relative risk of chondrolysis for purposes of general causation.

The Hansen/Beck Study reported surgical results of 152 shoulder arthroscopies. Pain pumps were inserted in 19 shoulder joints to deliver a continuous infusion of local anesthetics, and 12 of

those, or 63%, developed chondrolysis. Hansen/Beck Study, p. 1632. Patients who were not exposed to the continuous infusion did not develop chondrolysis, and the authors found no common factor in patients with chondrolysis except their exposure to continuous infusion. Id. Plaintiffs experts' Dr. Sander Greenland, an epidemiologist, and Dr. Martin Wells, a bio-statistician, opine that the Hansen/Beck Study, though published as a case series, is comprised of retrospective cohort data comparing the occurrence of chondrolysis in two patient populations - those who were exposed to continuous infusion and those who were not.<sup>9</sup> Based on their analysis, they assert that the high association between continuous infusion and chondrolysis reflected in the Hansen/Beck Study is statistically significant and cannot be attributed to chance. Defendants dispute the characterization of the Hansen/Beck Study as an epidemiological cohort study.

"Epidemiology is the field of public health and medicine that studies the incidence, distribution, and etiology of disease in human populations. The purpose of epidemiology is to better understand disease causation and to prevent disease in groups of individuals." REFERENCE MANUAL, p. 335. Epidemiology thus focuses on general rather than specific causation. Id. at 336. While "epidemiologic evidence can justify an inference that an agent causes a disease," id. at 336 n.8, "epidemiology cannot objectively prove causation; rather, causation is a judgment for epidemiologists and others interpreting the epidemiologic data." Id. at 374.

An epidemiological cohort study involves the study of two populations - or "cohorts" - to determine whether a population exposed to a particular agent is more likely to develop disease than the population which was not exposed. Id. at 340, 389. A retrospective cohort study occurs where

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<sup>9</sup>Plaintiffs also retained Drs. Greenland and Wells to analyze data underlying a case study conducted by Dr. Matsen. For reasons explained *infra*, I find Dr. Matsen's testimony unreliable and therefore any statistical analysis of his study is rendered moot.



"the researcher gathers historical data about exposure and disease outcome of the exposed cohort." Id. at 340 n.19. The possibility of bias and error is generally minimized through study design, usually developed before data is gathered, and involves selection of the study group under defined criteria. Id. at 341, 364, 371. A cohort study is considered Level II scientific evidence, while a case series is considered Level IV.<sup>10</sup>

It is undisputed that Dr. Beck did not design the Hansen/Beck Study as a Level II retrospective cohort and did not account for selection bias or confounding factors.<sup>11</sup> Greenland Dep., Sept. 24, 2009, p. 48 ("In fact, I know [Hansen and Beck] didn't take any procedures to try and adjust for possible selection bias."). Dr. Beck did not conduct epidemiological or statistical analysis, he did not consult with an epidemiologist, and he did not intend to "perform a Level II paper." Beck Dep., Aug. 31, 2009, p. 450. Rather, Dr. Beck reported on the occurrences of chondrolysis in his patients and "presented them for the review." Beck *Grossnickle* testimony, Mar. 3, 2009, Vol. 5B, p. 1225.

In other words, the Hansen/Beck Study was not designed as a "highly rigid, highly scientific study of A versus B." Id. In fact, Dr. Beck considers his study to be a Level IV case series, and it

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<sup>10</sup>Scientific evidence is assessed on a scale of Level I to Level V, with Level I granted the most scientific weight and Level V the least. A randomized controlled trial is an example of Level I evidence, prospective cohort studies are considered Level II evidence, retrospective cohort studies are examples of Level III evidence, case series are Level IV, and expert opinion is Level V. Editorial, *Introducing Levels of Evidence to The Journal*, 85 J. BONE & JOINT SURG. 1, 2 (Jan. 2003).

<sup>11</sup>"The meaning of scientific bias differs from conventional (and legal) usage" and "refers to anything . . . that results in error in a study and thereby compromises its validity." REFERENCE MANUAL, p. 363. "Selection bias refers to the error in an observed association that is due to the method of selection of . . . exposed and unexposed individuals (in a cohort study)." Id. at 363. "A confounding factor is both a risk factor for the disease and a factor associated with the exposure of interest." Id. at 369.

was published as such after a peer-review process. Beck Dep., Aug. 31, 2009, p. 445 (stating he had "no quarrel" with the Hansen/Beck Study published as a Level IV case series. "It is what it is."). Several experts in this litigation also consider the Hansen/Beck Study a Level IV case series.<sup>12</sup>

Although Drs. Greenland and Wells claim the Hansen/Beck Study data is similar to a Level II cohort, neither of them analyzed the underlying data of the study or performed independent analysis of potential biases or confounding factors. See Greenland Dep., Sept. 24, 2009, p. 91, 167-68. Further, Drs. Greenland and Wells both admit that the high association they discerned is limited to the patient population in the Hansen/Beck Study and cannot be generalized or applied to other patient populations who were exposed to continuous infusion. Finally, Dr. Greenland testified that the biggest limitation of the Hansen/Beck Study was its emphasis on continuous infusion without considering other potential causes of chondrolysis. Transcript of Proceedings, Nov. 18, 2009, p. 183, 212-13, 216-17; see also Wells Dep., Oct 5, 2009, p. 48-49. Thus, I find it questionable whether the Hansen/Beck Study constitutes helpful or relevant epidemiological evidence to support an opinion of general causation between continuous infusion and chondrolysis.<sup>13</sup>

Regardless, the lack of epidemiological evidence is not fatal to the admission of plaintiffs'

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<sup>12</sup>Though two experts believe that because of the comparison of populations, "it was approaching a Level III level of evidence"). Basamania Dep., Aug. 15, 2009, p. 512; Swanson Dep., Sept. 4, 2009, p. 321.

<sup>13</sup>In opposition to defendants' supplemental memorandum regarding Dr. Beck, plaintiffs present a letter written by a Dr. Samer Hasan to the American Journal of Sports Medicine. Dr. Hasan informs the editors that the Hansen/Beck Study is actually a Level II retrospective cohort study and proceeds to present his own statistical analysis of the data. O'Leary Decl. in Opp'n to Defs.' Suppl. Mem. re: Dr. Beck, Ex. 5, pp. 8-11. Aside from the fact that Dr. Hasan's letter cannot alter the character of the Hansen/Beck Study, Dr. Hasan is also retained by plaintiffs' counsel as an expert in other pain pump litigation. Horwitz Decl. in Supp. of Defs.' Suppl. Reply re: Dr. Beck, Ex. D.

experts' testimony, particularly in a case where no epidemiology "rules out" continuous infusion as a cause of chondrolysis. See W.R. Grace, 504 F.3d at 765 ("[T]he fact that a study is associational - rather than an epidemiological study intended to show causation - does not bar it from being used to inform an expert's opinion . . ."); Norris, 397 F.3d at 882 (epidemiological studies are not always necessary); Gladstetter v. Novartis Pharm. Corp., 252 F.3d 986, 992 (8th Cir. 2001) (accord); Kennedy, 161 F.3d at 1229 (finding expert's opinion reliable despite the lack of epidemiological studies linking Zyderm to atypical SLE); Grant v. Pharmative, 452 F. Supp. 2d 903, 908 (D. Neb. 2006); In re Ephedra, 393 F. Supp. 2d at 189-90 (explaining that "the absence of definitive scientific studies" should not "deprive a jury of having before it scientific opinions," though "less definitive and more qualified"); In re Phenylpropanolamine (PPA) Prods. Liab. Litig., 289 F. Supp. 2d 1230, 1242 (W.D. Wash. 2003) ("Non-epidemiological sources are frequently utilized by experts in rendering scientific opinions and, under *Daubert*, should be considered by the court in assessing the reliability of those opinions.").

Further, "[t]he human body is complex, etiology is often uncertain, and ethical concerns often prevent double-blind studies to calculate statistical proof." Primiano, 2010 WL 1660303, at \*5 (quoting Sandoval-Mendoza, 472 F.3d at 655). It is undisputed that chondrolysis is a rare disease, with few people exposed to potential causes and fewer actually developing the disease; consequently, "the opportunities for scholarly research are few. In such a situation, a lack of published studies should not bar otherwise scientifically valid testimony." Clausen, 339 F.3d at 1060. Moreover, ethical considerations preclude randomized, controlled epidemiological studies of continuous infusion given the potential for irreversible harm. Basamania Dep., Aug. 15, 2009, p. 434 ("[T]here will be no [prospective Level I, II, or III, studies] because it would not be ethical to perform those

studies based on what we know from our Level IV evidence."). Therefore, while epidemiological evidence is significant and can be helpful, it is not necessary to establish general causation.

## 2. Medical Studies Supporting Causation Opinions

Plaintiffs' experts universally rely on in vitro and animal studies demonstrating the chondrotoxic effects of local anesthetics and case series associating continuous infusion with chondrolysis. Defendants argue that plaintiffs' experts impermissibly extrapolate causal facts from these studies in a flawed attempt to support general causation.

### a. In Vitro and Animal Studies

Defendants take issue with several in vitro and animal studies cited by plaintiffs' experts, including those conducted by Drs. Dogan, Chu, Dragoo, Karpie, Gomoll, and Lo.

Dr. Dogan conducted animal studies involving the effects of bupivacaine when injected into the articular cartilage and synovium membranes of rabbit knee joints. Dogan, p. 513. Dr. Dogan observed "histopathological changes" to the joint and suggested that "physicians should be cautious when administering intra-articular bupivacaine." Id. at 518.

In her first study, Dr. Chu assessed the laboratory effects of 0.5% bupivacaine on bovine articular chondrocytes and found that such dosage was "cytotoxic" to bovine chondrocytes after 15 to 30 minutes of exposure. Dr. Chu concluded that while "the effects of bupivacaine on human cartilage may differ from the results obtained in vitro with bovine tissue, these results suggest that caution is needed in the intra-articular use of 0.5% bupivacaine solution." Chu I, p. 697. In her second study, Dr. Chu found that prolonged, continuous doses of bupivacaine increased the toxicity to human and bovine articular chondrocytes and asserted that "intra-articular bupivacaine should be used at the lowest dosage and for the shortest period of time necessary." Chu II, pp. 818-20.

Dr. Karpie, with Dr. Chu, conducted an in vitro study of bovine articular chondrocytes after exposure to lidocaine and found that "[a]lthough lidocaine chondrotoxicity was less than previously reported with bupivacaine, these data suggest a negative class effect of local anesthetics on articular chondrocyte viability." Karpie, p. 1626.

Ms. Piper and Dr. Kim studied the effects of bupivacaine and ropivacaine on human articular chondrocytes. The results of their study "demonstrate that a thirty-minute exposure to 0.5% bupivacaine is cytotoxic to human articular chondrocytes," both in intact cartilage and in cultured chondrocytes. Piper, pp. 989-90.

Similarly, Dr. Dragoo conducted research on the effects of bupivacaine on human cartilage cells harvested from patients undergoing knee replacement surgery. Dr. Dragoo noted that "[a]lthough a direct link of anesthetic-induced chondrolysis has not been established, multiple studies have shown the detrimental effects of local anesthetics on chondrocyte viability." Dragoo, p. 1484. Dr. Dragoo's study showed "significant loss of chondrocyte viability at all time points with medications containing epinephrine," particularly when exposed to 0.5% bupivacaine for 72 hours. Dragoo, p. 1487.

Dr. Lo analyzed the chondrotoxic effects of local anesthetics through the use of a bovine disk model. Dr. Lo concluded that local anesthetics such as bupivacaine can have "a detrimental effect on chondrocyte viability in a time and dose-dependent manner." Lo, pp. 709, 712, 714.

Finally, Dr. Gomoll conducted two animal studies on the toxic effects of bupivacaine injected into rabbit shoulder joints. In his 2006 study, Dr. Gomoll found that "[c]ontinuous intra-articular infusion of bupivacaine with and without epinephrine led to significant histopathologic and metabolic changes in articular cartilage." Gomoll I, p. 818. "In particular, bupivacaine showed

profound chondrotoxic effects in an experimental model that closely followed the current clinical application of postoperative pain pumps." Id. In his 2009 study, Dr. Gomoll found "no permanent impairment of cartilage function" three months after intra-articular infusion of bupivacaine in the rabbit shoulder model, although "20% to 30% of chondrocytes appeared nonviable 1 week after infusion with bupivacaine." Gomoll II, pp. 75-76.

Defendants maintain that plaintiffs' experts cannot reliably extrapolate data from these in vitro and animal studies to demonstrate causation in humans, particularly when the findings of the studies do not espouse a causal connection between continuous infusion and chondrolysis. See In re Bausch & Lomb, Inc. Contact Lens Solution Prods. Liab. Litig., 2009 WL 2750462, at \*12 (D.S.C. Aug. 26, 2009) ("In vitro tests generate hypotheses but lack sufficient reliability, standing alone, to demonstrate causation in humans."). Defendants emphasize that the studies' authors themselves cautioned against extrapolating the results to humans in a clinical setting.

However, "analogy, inference and extrapolation can be sufficiently reliable" when the expert's opinion is the "kind that a reasonable scientist or physician would make in a decision of importance arising in the exercise of his profession outside the context of litigation." In re Ephedra, 393 F. Supp. 2d at 189. Without question, physicians consider "the medical and scientific literature as well as information about a patient's condition to best determine causality." REFERENCE MANUAL, p. 470; Metabolife Int'l, Inc. v. Wornick, 264 F.3d 832, 842 (9th Cir. 2001) (noting that animal studies can provide "useful data about human health."). In fact, many of the peer-reviewed articles cited by plaintiffs and their experts include discussions of in vitro and animal studies, including those conducted by Dr. Chu and Dr. Gomoll. Several articles not only cite Dr. Chu's studies, but give credence to the correlation between chondrocyte damage and exposure to local anesthetics. See, e.g.,

Greis, p. 1343; see also Hopkins v. Dow Corning, Corp., 33 F.3d 1116, 1125 (9th Cir. 1994) (finding admissible testimony based on scientific studies and "corroborating evidence found in studies conducted on animals"); In re Silicone Gel Breast Implants Prods. Liab. Litig., 318 F. Supp. 2d 879, 910-11 (C.D. Cal. 2004) (noting reliance by researchers and agencies on relevant animal studies). Thus, defendants cannot credibly argue that the reliance on in vitro and animals studies is scientifically invalid in this case. Whatever inadequacies arise from extrapolation will no doubt be addressed through vigorous cross-examination by defense counsel.

I further find that the cited in vitro and animal studies lend support to the opinions of plaintiffs' experts by establishing the chondrotoxicity of local anesthetics. Such toxicity is significant given that chondrolysis results from the degeneration and eventual death of cartilage cells. Solomon, p. 1330. Granted, plaintiffs' experts are not certain why bupivacaine is chondrotoxic or how the damage is caused, though some opine that displacement of the synovial fluid robs the cartilage matrix of nutrients necessary for its renewal. See infra, pp. 64, 69-70. However, "[n]ot knowing the mechanism whereby a particular agent causes a particular effect is not always fatal to a plaintiff's claim. Causation can be proved even when we don't know precisely *how* the damage occurred, if there is sufficiently compelling proof that the agent must have caused the damage *somehow*." Daubert II, 43 F.3d at 1314; Domingo ex rel. Domingo v. T.K., 289 F.3d 600, 607 (9th Cir. 2002) ("[I]t is not necessary to show *how* a particular act or event caused an injury."); see also Primiano, 2010 WL 1660303, at \*5 ("Lack of certainty is not, for a qualified expert, the same thing as guesswork."); In re Neurontin Mktg. Sales Practices & Prods. Liab. Litig., 612 F. Supp. 2d 116, 149 (D. Mass.2009) ("biologic plausibility" supported opinion on causation despite "robust debate in the scientific community" on the proposed mechanism); In re PPA, 289 F. Supp. 2d at 1247 ("The fact

that the mechanism remains unclear does not call the reliability of the opinion into question.”).

The cited studies also demonstrate a basic dose-response relationship in that higher doses and longer exposure to bupivacaine result in increased chondrotoxicity. See Chu I, pp. 693, 696; Chu II, pp. 814, 818-20; Dragoo, pp. 1487-88; see also Badylak Dep. July 27, 2009, pp. 328, 349 ("I think everybody would agree the higher the dose and the longer exposure, the worse you're going to get. So we understand the relationship to be dose depend - dose and time dependent. What we don't know is what the - the threshold is. We don't know what - what's too much."). While plaintiffs' experts cannot identify the precise threshold dose of bupivacaine or the length of exposure that triggers irreparable chondrocyte damage, "*Daubert* does not require that every aspect of a theory of medical causation be supported by research on the identical point." Domingo, 289 F.3d at 607 (quotation marks and citation omitted); see also Westberry, 178 F.3d at 264 (the precise "exposure necessary to cause specific harm to humans" is not "always available, or necessary, to demonstrate" toxicity and "need not invariably provide the basis for an expert's opinion on causation") (quoted with approval in Clausen, 339 F.3d at 1058-59).

Defendants next argue that plaintiffs' experts failed to reconcile their opinions with Gomoll II. Defendants are not entirely correct. In particular, Dr. Badylak, when asked if Gomoll II did not support the finding that local anesthetics were chondrotoxic, explained:

Oh no, I - just the opposite. It is chondrotoxic. What [Gomoll's] 2000 – his 2006 study showed it was chondrotoxic, so he did the 2009 study to - to look for longer terms. He doesn't change his opinion that it's not chondrotoxic. What he says in the 2009 [study] is that in the model that was used, which was [sic] these young rabbits, that perhaps a reparative response was - was taking place and that we should not necessarily extrapolate that to humans.

Badylak Dep. July 27, 2009, p. 286; see also Dragoo Dep., June 12, 2009 pp. 207-08, 228



(explaining that rabbits can regenerate cartilage tissue). Whether other physicians, such as Dr. Basamania, interpret Gomoll II differently is properly addressed on cross-examination. See Basamania Dep., Aug. 15, 2009, p. 474.

I recognize that, as Dr. Badylak conceded, in vitro and animal studies are not "perfect." Badylak Dep., July 27, 2009, p. 287 ("There is - until you do the human clinical trial, you just never know."). However, such studies are relied on in the medical profession and provide useful information, as Dr. Dragoo explained:

[B]y ethical standards, we cannot [test for the chondrotoxicity of local anesthetics] in [a live] human model. So therefore, we will use an animal model, and therefore, we would have to extrapolate to say that the animal models are a good reflection of what happens in a human. Well, they both have their ups and downs. So what we have done as a collective whole in science is to do both. My studies focus on human cells with a reasonable bioreactor condition to mimic what goes on. And [Gomoll] then used the animal model. Well, what's the down side of his model, Well, the good news is that it's a living model. The bad news is that it's a rabbit and it's not a human. So there, we're getting the best we can in finding the answers. If we could do this on live humans, we would. But we're not allowed to do that ethically.

Dragoo Dep., June 12, 2009, p. 218. Contrary to defendants' position, *Daubert* recognizes that expert opinion can only be based on "what is known." Thus, "[t]he grounds for the expert's opinion merely have to be good, they do not have to be perfect." In re Paoli, 35 F.3d at 744.

Here, the cited studies demonstrate that prolonged exposure to local anesthetics causes damage to cartilage cells, thus informing as well as supporting the opinions of plaintiffs' experts and providing independently reliable evidence that continuous infusion causes harm to cartilage. "Although these sources [may] not definitively prove causation or establish a mechanism of toxicity, they are a sufficient basis upon which to base a medical opinion." Golod v. LaRoche, 964 F. Supp. 841, 858 (S.D.N.Y. 1997).

b. Case series

Defendants also challenge plaintiffs' experts' reliance on several case series, most notably the 2007 case series co-authored by Dr. Beck. Defendants contend that case studies are merely compilations of occurrences with low scientific value, particularly when the series do not and cannot establish that continuous infusion causes chondrolysis.

Based on the number of patients with pain pumps who developed chondrolysis, the Hansen/Beck Study asserts that a "strong association" exists between continuous infusion and chondrolysis, while acknowledging that the exact cause of chondrolysis is undetermined and that "other unrecognized factors are also involved." Hansen/Beck Study, p. 1633. Other case series cited by plaintiffs' experts similarly discuss continuous infusion as a cause of chondrolysis. See Greis, pp. 1338-1344; Busfield, p. 651; Fester, p. 6; Saltzman, p. 3; Rapley et al., *Glenohumeral Chondrolysis After Shoulder Arthroscopy Associated With Continuous Bupivacaine Infusion*, 12 ARTHROSCOPY: J. ARTHROSCOPIC & RELATED SURG. 1367 (Dec. 2009). In Rapley, for example, the authors studied the incident rate of chondrolysis in patients after the use of pain pumps to administer local anesthetics. The authors initially hypothesized that chondrolysis was "uncommonly associated with [continuous infusion device] use in the glenohumeral joint." Rapley, p. 1367. However, of 16 patients receiving high-volume continuous infusion, 3 developed chondrolysis, while none of the 13 patients receiving either low-volume continuous infusion or local anesthetics outside the joint space developed chondrolysis. Id. at 1372. The authors thus concluded that their hypothesis was "refuted," because "a 20% incidence of glenohumeral chondrolysis cannot be considered 'uncommon.'" Id.

In a rather compelling abstract, Saltzman reported the case of a patient with injuries to both shoulders. Saltzman, p. 1. The patient underwent an arthroscopic procedure on the right shoulder,

and an intra-articular pain pump catheter was placed for the continuous infusion of lidocaine. Id. at 2. However, "the pain pump never functioned properly, as evidenced by continuous leakage outside of her body until its removal several days later." Id. Several months later, the patient underwent arthroscopy on her left shoulder, and again an intra-articular pain pump was used to continuously infuse lidocaine at the same dosage rate. The pain pump did not leak and "appeared to function as intended for several days after the procedure." Id. Several months afterward, the left joint area was "noted to be nearly completely devoid of articular cartilage." Id. The patient was eventually diagnosed with chondrolysis in the left shoulder joint, while her right joint space appeared normal. Id. The authors noted that the "main difference" between the two shoulder procedures was a functioning pain pump in the left shoulder joint that developed chondrolysis and a non-functioning pain pump in the right shoulder that did not development chondrolysis. Id. at 3.

Admittedly, case series are not afforded a high level of scientific weight, as they generally report and describe clinical occurrences without attempting to control for certain variables, such as selection bias or other potential causal factors. REFERENCE MANUAL, p. 475; see Casey v. Ohio Med. Prods., 877 F. Supp. 1380, 1385 (N.D. Cal. 1995). Further, defendants are correct that several case series advise that the cause and etiology of chondrolysis are not fully understood. See, e.g., Bailie, p. 2 ("[T]he actual cause of even the reported cases [of chondrolysis] has not been confirmed and the associations are speculative at this juncture."); Solomon, p. 1339 ("After careful examination, the aggregate evidence across studies suggests that the development of [glenohumeral chondrolysis] is multifactorial.").

That said, the cited case reports provide ample evidence of an association between continuous infusion and chondrolysis. The fact that case series are not given ultimate weight as

scientific evidence does not render them unreliable as a source of expert testimony. Kennedy, 161 F.3d at 1229-30; In re PPA, 289 F. Supp. 2d at 1242. As with in vitro and animal studies, case series are routinely reviewed and relied upon by physicians in the normal course of their profession, as evidenced by a review of the medical literature. Bailie, pp. 4-5; Busfield, pp. 648-51; Chu I, p. 699; Fester, p. 6; Greis, pp. 1342-43; Kang, p. 913; REFERENCE MANUAL, p. 470, 473-74. In fact, a defense expert believes that chronic synovitis following blood in the joint space can cause chondrolysis, based on his review of case series. Stetson Dep. Aug. 25, 2009, pp. 16-17. A second defense expert opines that numerous other factors may cause chondrolysis, including gentian dye, thermal wands, a patient's age, and suture anchors, based on isolated occurrences reported in case series. Burkhead Dep. Aug. 31, 2009, pp. 30, 34-36, 39, 47-48, 144-46.

Finally, the studies' "failure to establish causation goes to the weight it should be accorded, but does not mean that an expert could not rely on it in forming an opinion." W.R. Grace, 504 F.3d at 765. Thus, defendants' assorted grievances with the cited case series are properly addressed through the adversary process.

### 3. Whole of Medical Evidence

Finally, defendants contend that plaintiffs' experts employ unreliable methodologies by "cherry-picking" facts from certain studies and asserting reliance on the "totality" or "global gestalt of medical evidence." Defendants argue that in doing so, plaintiffs' experts fail to "painstakingly" link each piece of data to their conclusions or explain how the evidence supports their opinions.

Defendants are correct that plaintiffs' experts must elucidate how the relevant evidence lends support to their opinions by explaining "precisely how [they] went about reaching their conclusions and point[ing] to some objective source . . . to show that they have followed the scientific method,

as it is practiced by (at least) a recognized minority of scientists in their field." Domingo, 289 F.3d at 605-06 (quotation marks and citation omitted). An expert's obligation to explain the basis for a proffered opinion does not mean that each piece of data must support causation when considered in isolation. To the contrary, physicians routinely consult multiple sources of data in the normal course of their practices. Heller, 167 F.3d at 155-56; Kennedy, 161 F.3d at 1228-30; In re PPA, 289 F. Supp. 2d at 1242; RESEARCH MANUAL, 470.

In fact, the Ninth Circuit found erroneous a district court's "document-by-document Rule 702 analysis" that effectively "deconstructed" an expert's testimony "in a manner not contemplated by Rule 702." W.R. Grace, 504 F.3d at 765. Instead, evaluation of an expert's opinion testimony "requires consideration of the *overall* sufficiency of the underlying facts and data, and the reliability of the methods, as well as the fit of the methods to the facts of the case." Id.; accord Clausen, 339 F.3d at 1058-59 (emphasizing the totality and "variety" of the "objective, verifiable evidence" considered by the expert); In re PPA, 289 F. Supp. 2d at 1242 ("Defendants isolate these sources, rather than considering the whole.").

Moreover, plaintiffs' experts explained that in forming their opinions they considered in vitro and animal studies establishing the chondrotoxicity of local anesthetics, case reports presenting evidence of an association between continuous infusion and chondrolysis, and the temporal relationship between the continuous infusion and the increased reports of chondrolysis.<sup>14</sup> See

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<sup>14</sup>Defendants also complain that plaintiffs' experts did not adequately elucidate each step of their methodologies within the "four corners" of their expert reports. The purpose of expert reports is to "avoid unfair surprise by enabling the adversary to prepare a response to the expert testimony." Cohen v. Lockwood, 2004 WL 763961, at \*4 (D. Kan. Apr. 8, 2004); see Walsh v. Chez, 583 F.3d 990, 994 (7th Cir. 2009) (purpose of reports "is not to replicate every word that the expert might say on the stand" but "to convey the substance of the expert's opinion"). The Ninth Circuit has approved, albeit implicitly, an explanation of an expert's methodology offered

Badylak Dep., July 27, 2009, pp. 325-26 ("You combine [the Hansen/Beck Study] with the other experiences, the in vitro data, the pre-clinical studies and so forth . . . this becomes a no-brainer, frankly."). In sum, the proffered expert opinions "rest on more than simply the 'ipse dixit' of the experts." In re PPA, 289 F. Supp. 2d at 1248.

I thus find that reliance on and reference to the totality of medical evidence is a valid methodology, and that the evidence cited by plaintiffs' experts sufficiently, even if not conclusively, supports their opinions. "[W]eaknesses in the methodology and investigation of [a] particular expert might lead the trier of fact to discount his opinions,' but '*Daubert* only prescribes judicial intervention for expert testimony approaching the outer boundaries of traditional scientific and technological knowledge.'" Golod, 964 F. Supp. at 858 (quoting Lappe v. Am. Honda Motor Co., 857 F. Supp. 222, 228 (N.D.N.Y. 1994)). The methodologies of plaintiffs' experts hardly reach the outer boundaries of medical knowledge to justify exclusion of their testimony.

### C. Other Factors Bearing on Reliability

Defendant also argue that the testimony of plaintiffs' experts bear no other hallmark of scientific validity, because they lack peer review, general acceptance and are driven by litigation.

#### 1. Peer Review

Defendants assert that the opinions of plaintiffs' experts avowing a causal relationship between continuous infusion and chondrolysis have not been subjected to peer review, unlike their equivocal research opinions on the cause of chondrolysis. Daubert, 509 U.S. at 593. Defendants

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in deposition. Kennedy, 161 F.3d at 1230 ("Dr. Spindler set forth the steps he took in arriving at his conclusion in his deposition."). Given the numerous, lengthy, and altogether comprehensive depositions of plaintiffs' experts, any infirmity in an expert's report is not prejudicial and does not warrant exclusion.

suggest that plaintiffs' experts' unwillingness to submit their causation theories to peer review reveals the scientific unworthiness of their testimony and warrants the inference that their opinions are not based on "good science." I disagree.

As I indicated at oral argument on March 17, 2010, there are many reasons why an expert may not engage in academic research or present an expert opinion for peer review. Transcript of Proceedings, Mar. 17, 2010, pp. 104-05. Other reasons may explain why an opinion given as an expert reaches a stronger conclusion than one given as a researcher. As Dr. Dragoo explained:

[I]n the medical literature and in the medical peer-reviewed literature, statements outside the direct boundaries of research [are] not allowed. And that's the difference between the facts and the statements that are presented in the scientific literature and professional opinion or what is happening beyond this [study], because this is just a reflection of the exact study that was here, and not incorporating all of the other factors that are required for evaluation of the development of chondrolysis. So it cannot be stated in here. Do I think it is a causative factor? Yes, but it is not stated in here by convention.

Dragoo Dep. June 12, 2009, p. 50. Even if the opinions of plaintiffs' experts lack peer review, I do not find their opinions unreliable on that basis.

Peer review is not an absolute prerequisite for the admission of expert testimony. Rather, "[i]n the absence of independent research or peer review, experts must explain the process by which they reached their conclusions and identify some type of objective source demonstrating their adherence to the scientific method." In re PPA, 289 F. Supp. 2d at 1238 (citing Daubert II, 43 F.3d at 1318-19 and Domingo, 289 F.3d at 605-06). Thus, even if an expert's research is not "subjected to normal scientific scrutiny through peer review and publication," the "proffer of scientific testimony may still be deemed reliable enough to be admitted." Clausen, 339 F.3d at 1056.

As explained above, plaintiffs' experts identify objective, scientific sources and sufficiently

explain how the evidence supports their opinions. Thus, the lack of peer review is an appropriate topic for cross-examination rather than grounds for exclusion.

## 2. General Acceptance

Defendants next argue that plaintiffs' experts' opinions are not "generally accepted" within the medical or scientific communities, because (again) no peer-reviewed, medical study concludes that continuous infusion causes chondrolysis. Aside from my finding that reliable evidence of general causation does not require conclusive or undisputed evidence, it is not the experts' *opinions* that are assessed for general acceptance. Rather, "[t]he focus under *Daubert* is on the reliability of the methodology, and in addressing that question the court and the parties are not limited to what is generally accepted; methods accepted by a minority in the scientific community may well be sufficient." Daubert II, 43 F.3d at 1319 n.11.

Most of plaintiffs' experts adopt similar methodologies: reliance on their knowledge and clinical experience combined with review of the relevant medical literature and, in most cases, medical records of patients with chondrolysis. I find that such methods are generally accepted in the medical field.

Physicians rely on their training and expertise as clinicians and scientists when considering the medical and scientific literature as well as information about a patient's condition to best determine causality in a particular patient. Definitive tests for causality are actually rare, and physicians must almost always use an element of judgment in determining the relationship between exposure and disease in a given patient.

REFERENCE MANUAL, pp. 470-71. As recognized recently by the Ninth Circuit, a medical expert's methodology of comparing "what happened" to a patient with what physicians "ordinarily see, against a backdrop of peer-reviewed literature, is the ordinary methodology of evidence based



medicine[.]" Primiano, 2010 WL 1660303, at \*6 (quotation marks and citations omitted).

Furthermore, I physicians apparently no longer use pain pumps for intra-articular continuous infusion, and a medical textbook warns against using pain pumps for continuous infusion, stating that "there is a growing body of evidence linking intra-articular infusion of bupivacaine . . . via pain pump to postoperative chondrolysis." THE SHOULDER, 918 (4th ed. 2009) (O'Leary Decl. in Supp. of Mot. to Exclude Defs.' Experts, Ex. 38).<sup>15</sup> Several authors of case studies likewise counsel against the use of continuous infusion, and the FDA issued a similar warning.

From this evidence, it can be inferred that the medical community generally accepts not only the methodology relied on by plaintiffs' experts, but their conclusions that continuous infusion can cause chondrolysis. In fact, Dr. Bailie, an author of a cited case series, testified that continuous infusion is "strongly suspected" to be the primary cause of chondrolysis, to the extent that "it's accepted to be cause and effect in the orthopedic community." See Bailie Dep., Sept. 25, 2009, p. 162.

Defendants respond that clinical recommendations against the use of continuous infusion are not scientific evidence of general acceptance, because doctors do not engage in scientific methodology when making decisions based on patients' safety. See Siharath, 131 F. Supp. 2d at 1372 (finding clinical recommendations insignificant with respect to the general acceptance of scientific methodology). Defendants' argument begs the question of whether they ascribe to physicians a level of "intellectual rigor" that does not accurately characterize the typical decision-

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<sup>15</sup>Defendants maintain that the evidentiary value of this medical text is lessened by Dr. Matsen's involvement as an editor. However, given that the text has authors and editors unrelated to this litigation, I do not find that Dr. Matsen's involvement renders this text unreliable as a source.

making process of the profession. See Kumho, 526 U.S. at 152; Primiano, 2010 WL 1660303, at \*4 ("Despite the importance of evidence-based medicine, much of medical decision-making relies on judgment - a process that is difficult to quantify or even to assess qualitatively.") (quotation marks and citation omitted). Regardless, I find that such clinical recommendations bolster the general acceptance of the methodologies employed by plaintiffs' experts.

### 3. Litigation Bias

Finally, defendants argue that plaintiffs' experts' opinions are products of litigation rather than independent research, given the lack of scientific evidence concluding that continuous infusion causes chondrolysis. As explained above, reliable testimony does not require conclusive evidence of causation, and its absence does not mandate the assumption that plaintiffs' experts are driven by the prospect of compensation for their litigation efforts.

That said, defendants are correct that the majority of plaintiffs' experts developed and articulated their general causation opinions after being retained as experts. Further, no expert aside from Drs. Beck and Dragoo conducted independent studies involving chondrolysis.<sup>16</sup> Nevertheless, the fact that an expert's opinion may be obtained for purposes of litigation does not render it unreliable if otherwise supported by "objective, verifiable evidence that the testimony is based on

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<sup>16</sup>As discussed, Dr. Beck reviewed records of patients who developed chondrolysis and co-wrote a paper analyzing his findings, and Dr. Dragoo conducted independent laboratory research on the toxicity of local anesthetics to human cartilage cells. Additionally, plaintiffs claim that Drs. Badylak and Basamania conducted independent research. Dr. Basamania reviewed records of several patients who developed chondrolysis after arthroscopic shoulder surgery. Two days before presenting his findings, Dr. Basamania revised his presentation to conclude that continuous infusion was a causal factor of chondrolysis. Dr. Badylak apparently "borrowed" cartilage tissue from his colleague, Dr. Chu, to verify that exposure to bupivacaine causes chondrotoxicity. Given these circumstances, I do not find that Dr. Basamania's presentation or Dr. Badylak's experiment constitutes "research."

'scientifically valid principles.'" Daubert II, 43 F.3d at 1318; see also Clausen, 339 F.3d at 1056 (even though expert's research was not "conducted independent of the litigation" and his opinion was developed "expressly for purposes of testifying," expert's testimony was not improperly admitted). Instead, this factor is one of several a court must consider in determining reliability.

Defendants also claim that many of plaintiffs' experts' reports were drafted by counsel in violation of Federal Rule of Civil Procedure 26 (Rule 26). In particular, defendants emphasize that portions of the expert reports of Drs. Beck and Basamania are similar if not identical.

The Advisory Committee Notes to Rule 26 provide that an expert report "should be written in a manner that reflects the testimony to be given by the witness and it must be signed by the witness." Thus, Rule 26 does not prohibit counsel's assistance in preparing or drafting an expert report. Trigon Ins. Co. v. United States, 204 F.R.D. 277, 292 (E.D. Va. 2001). At the same time, an expert report "ghost-written" from "whole cloth" violates the spirit, if not the letter of the Rule, as do reports that have been altered by counsel or prepared "merely for appeasement or because of intimidation or some undue influence by the party or counsel who has retained him." Id. at 292-93 (quotation marks and citation omitted). Finally, expert reports may be discredited if they "merely express the opinions of the lawyers who hired them." Id. at 294. To this end, one district court struck an expert report that was "remarkably similar" to two others "in their language and conclusions." Id. at 293-94 (citing In re Jackson Nat'l Life Ins. Co. Premium Litig., 2000 WL 33654070 (W.D. Mich. Feb. 8, 2000)).

Whether counsel's assistance in preparing an expert report violates Rule 26 is a fact-specific inquiry. Generally, I find no more than acceptable editorial assistance from counsel. To the extent counsel's involvement flirted with the outer boundaries of Rule 26, I consider the above principles

when discussing each expert's opinion.

#### D. Defendants' Challenges Against Individual Expert Witnesses

Defendants do not challenge the credentials of plaintiffs' experts or otherwise argue that they are unqualified to render expert medical opinions. Rather, defendants argue that the methodologies employed by them are unreliable and mandate exclusion of their testimony.

##### 1. Dr. Frederick Matsen

Dr. Matsen is a board-certified orthopedic surgeon, professor, and until very recently, the Chairman of the Department of Orthopedic Surgery and Sports Medicine at the University of Washington School of Medicine in Seattle, Washington. Dr. Matsen obtained his medical degree from Baylor University College of Medicine, completed a surgical internship at Johns Hopkins University and performed medical research for two years at the National Institutes of Health. Dr. Matsen completed his residency at the University of Washington in 1975 and has since remained on the faculty. Dr. Matsen has been retained as an expert witness by plaintiffs in this and other pain pump litigation and intends to offer testimony that continuous infusion can cause glenohumeral chondrolysis. Matsen Expert Report, p. 13.

Defendants challenge Dr. Matsen's on numerous grounds, including the ever-changing and unfinished study that is the basis of his opinion, and the inherent selection and litigation bias in the study. Defendants also move to strike Dr. Matsen's testimony pursuant to Rules 26 and 37, based on the failure to disclose and produce e-mail communications between Dr. Matsen and Mr. Wihtol that discuss their analysis of patient records involved in the chondrolysis study. Given the circumstances, I agree that Dr. Matsen's opinion fails to reach the threshold of reliability.

Dr. Matsen, though an experienced orthopedic surgeon, has little if any experience with

arthroscopies, and he has never used a pain pump during any surgical procedure. Matsen Dep., Feb. 17, 2010, p. 741 ("I don't do shoulder arthroscopy and have never used a pain pump."). In fact, when first contacted by Mr. Wihtol in mid-2007, Dr. Matsen stated he had no experience in the area of chondrolysis. Id. at 794; Hall Decl. Re: Pls.' Arg., Ex. V. Mr. Wihtol apparently convinced Dr. Matsen to participate as an expert witness and offered to provide patient data for a study on potential causes of chondrolysis.

In his original expert report, Dr. Matsen cites as support for his opinion a case study of 67 patients (the 67-study), a case study of 396 patients (the 396-study), and his treatment of one patient with glenohumeral chondrolysis. Matsen Report, p. 3.

The 67-study described the cases of patients who developed chondrolysis after arthroscopic shoulder surgeries performed by Dr. Benz, a Portland, Oregon surgeon, during which pain pumps were inserted intra-articularly to administer bupivacaine. The idea for the study originated with Mr. Wihtol, who provided Dr. Matsen with patient records he had obtained from Dr. Benz during the course of a state court pain pump litigation.<sup>17</sup> Matsen Report, pp. 4-6; Matsen Dep. Jan. 28, 2010, p. 460. Dr. Matsen presented the 67-study for publication in a peer-reviewed journal, but it was repeatedly rejected because of selection and litigation bias. Journal reviewers were concerned that Dr. Matsen provided no information about the population from which the 67 patients were selected and that the patient data had been obtained from a law firm. Matsen Dep. Feb. 17, 2010, p. 747.

Dr. Matsen recently disclaimed any reliance on the 67-patient study and acknowledged its inherent limitations associated with the selection of the patient data. Matsen Dep. Sept. 4, 2009, p.

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<sup>17</sup>Dr. Benz was a defendant in the *Grossnickle* state court action brought by several patients after they developed chondrolysis, though he eventually settled with each of them. Mr. Wihtol was counsel for the plaintiffs in that lawsuit.

18 ("I am not knowledgeable about the population from which those 67 cases came, so I don't think that that particular series of case reports . . . has the scientific basis for an opinion on causation because of the way those cases were gathered."). Dr. Matsen also conceded that his experience treating one chondrolysis patient was insufficient as a basis for his causation opinion. Id. p. 239 ("I don't think I have enough experience treating chondrolysis patients to make conclusions.").<sup>18</sup> Aside from medical literature, the remaining support for Dr. Matsen's opinion is the 396-study. I thus look to the 396-patient study as the primary basis of his opinion.

After the 67-study was rejected for publication, Mr. Wihtol and Dr. Matsen developed the idea for the 396-study to address the concern of selection bias. Mr. Wihtol offered to provide Dr. Matsen with a more complete set of patient data and obtained patient records from arthroscopic surgeries performed by Dr. Benz between 1996 to 2008.<sup>19</sup> Matsen Dep. Jan. 28, 2010, p. 460 ("[T]he idea for the study came up in a conversation that I had with Mr. Wihtol and I asked if he could get access for us to these primary source documents from Dr. Benz's practice. He said he could."). Dr. Matsen's expert report thus describes the 67-study as the "father" of the 396-study "specifically

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<sup>18</sup>Dr. Matsen also disavowed the statement in his expert report that continuous infusion of local anesthetics "*in volumes of 250 ml. more or less over a period of 2-3 days or more*, is a scientifically plausible cause of glenohumeral chondrolysis." Matsen Expert Report, p. 13 (emphasis added). Dr. Matsen admitted that he did not analyze dosages or flow rates of anesthetics. Matsen Dep. Feb. 17, 2010, p. 786 ("With all respect, I don't remember making a statement about knowledge of specific volumes. . . . If I said that, I perhaps should reconsider that statement."). That Dr. Matsen admits never asserting an opinion on dosage or flow rate is troubling in and of itself and raises questions about the authorship of his expert report.

<sup>19</sup>The exact number of patients involved in this study remains unclear to the court. Although most often referred to as the 396-patient study, apparently only 375 patients out of 404 were included (instead of 396). Additionally, the initial data transmitted to Dr. Matsen included approximately 600 patients, and Dr. Matsen cannot account for the reduction of patients. Matsen Dep. Jan. 28, 2010, p. 474 ("I cannot account to you why the difference in numbers between 600 and 404 . . ."). In the interest of consistency, I refer to it as the 396-study.

designed to evaluate the cause or causes of glenohumeral chondrolysis." Matsen Expert Report, pp. 4, 5.

Those conducting the 396-study included Dr. Matsen, Sue Moerer, a nurse who extracted data from the patient records, and Dr. Brett Wiater, a resident physician at the University of Washington who analyzed the data. Mr. Wihtol contacted Ms. Moerer about participating in the study, as she had performed similar work for him in the past and previously redacted the Benz patient records. Moerer Dep. Jan. 21, 2010, pp. 37, 41-43. Dr. Matsen ultimately hired Ms. Moerer to extract data, although he did not request information regarding her qualifications or references. Matsen Dep. Feb. 17, 2010, p. 806. Based on data extracted from the Benz patient records and his analysis of the number and percentage of patients who developed glenohumeral chondrolysis after receiving intra-articular continuous infusion, Dr. Matsen concludes that continuous infusion causes chondrolysis.

Defendants maintain that the 396-study is fundamentally flawed as a result of selection bias and the influence of litigation. Although selection bias in the 396-study is a concern, I find that litigation bias is ultimately what renders Dr. Matsen's testimony unreliable.<sup>20</sup>

Dr. Matsen repeatedly asserts that he undertook the 396-study without a preconceived opinion about the role of continuous infusion, and that his intent was to explore other potential causes of chondrolysis. Matsen Dep. Feb. 17, 2010, p. 722 ("We wanted to look at the data . . . fresh so that it wasn't like we have a mission here, we have a vested interest, or a hypothesis."). However,

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<sup>20</sup>Defendants assert selection bias, in part, based on follow-up letters sent only to patients who received continuous infusion requesting that they return for a chondrolysis evaluation, and the limited temporal scope of the study precluding detection of potential cases of chondrolysis in patients who had shoulder arthroscopy in 2007 and 2008. Given my exclusion of Dr. Matsen's testimony on other grounds, I need not address these arguments.

plaintiffs retained Dr. Matsen as an expert before the 396-study's genesis in early 2009, and Dr. Matsen had no prior experience in arthroscopy or knowledge of chondrolysis. Thus, not only was Dr. Matsen's opinion developed for purposes of litigation, the study that was intended to support his opinion was designed and conducted during the course of litigation. See Daubert II, 43 F.3d at 1317 (independent, pre-litigation research "provides important, objective proof that the research comports with the dictates of good science" and is less likely "to have been biased by the promise of remuneration").

Moreover, Dr. Matsen admits that the 396-study remains unwritten and unfinished as of February 2010, even as it was the purported basis for his expert testimony rendered in two state court cases. See Matsen Dep. Jan. 28, 2010, pp. 345-46; Matsen Dep., Feb. 17, 2010, p. 645. Dr. Matsen also concedes that defense counsel recently identified omissions in the study's analysis, and that the final "numbers" will likely change. Matsen Dep. Feb. 17, 2010, pp. 799-800. Plaintiffs do not dispute that Dr. Matsen "undertook his investigation in the course of litigation and his analysis has not yet been published." Pls.' Opp'n to Defs.' Combined Mots. to Exclude Matsen, p. 22. That Dr. Matsen agreed to assert a causation opinion in this and other litigation - *prior to the conclusion of his study that purportedly forms the basis of his opinion* - evinces a preconceived belief that is not supported by a reliable, or even identifiable, basis. Benkwith v. Matrixx Initiatives, Inc., 467 F. Supp. 2d 1316, 1325 (M.D. Ala. 2006) (based on its timing, finding an expert's experiment "appears to have been undertaken more to bolster a conclusion than to test a hypothesis"). Aside from the amorphous basis of Dr. Matsen's opinion, litigation bias associated with the 396-study renders his testimony unreliable.

At the outset, the circumstances under which the 396-study evolved give the court pause.



First, the idea for the 396-study originated in part with Mr. Wihtol, who was and is counsel for plaintiffs in this and other pain pump litigation. Second, the patient data for the study was provided by Mr. Wihtol. Third, Mr. Wihtol obtained the patient data from Dr. Benz, a surgeon whose patients experienced a high incidence of chondrolysis after arthroscopic shoulder surgery and who entered into settlement agreements with patients who were represented by Mr. Wihtol.<sup>21</sup> Fourth, Mr. Wihtol provided the records in electronic format to Ms. Moerer, the nurse recommended by Mr. Wihtol to conduct data extraction. Moerer Dep. Jan 21, 2010, pp. 43, 46-47; Horwitz Decl. in Supp. of Renewed Mot. to Strike Matsen, Ex. E, pp. 14-16. Finally, Mr. Wihtol and Dr. Matsen developed the idea for the study and compiled the data to support it after Mr. Wihtol retained Dr. Matsen as an expert witness and during the course of litigation. These facts alone raise the disquieting specter of litigation bias.

The shadow cast over Dr. Matsen's opinion looms larger and darker after the disclosure of e-mail communications between Mr. Wihtol and Dr. Matsen that discuss the patient data of the 396-study.

As stated, Sue Moerer is the nurse selected and recommended by Mr. Wihtol to extract data from the Benz patient records. Pursuant to her deposition subpoena in January 2010, she produced e-mail communications between and among herself, Dr. Matsen, and Dr. Wiater. Within these e-

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<sup>21</sup>According to Dr. Matsen's study of the data, forty-nine of Dr. Benz's patients developed chondrolysis after arthroscopic shoulder surgery, a significantly higher number than that associated with other physicians. Matsen Expert Report, p. 9. In the *Grossnickle* state court action, Dr. Benz entered into a "Covenant Not to Enforce Judgment and Separate Loan Agreement" on June 20, 2008, in which several pain pump plaintiffs settled their claims against Dr. Benz in exchange for payment of monies. Dr. Benz also agreed to loan a certain sum of money to each plaintiff "to help Plaintiffs finance the litigation against Stryker and I-Flow." Hall Decl. Re: Pls.' Arg., Ex. Q, pp. 5-8.

mail communications are conversation threads between Dr. Matsen and Mr. Wihtol reflecting a degree of involvement by counsel that goes far beyond providing information.

The following e-mail exchanges exemplify Mr. Wihtol's involvement in the 396-study:

Message from Dr. Matsen to Mr. Wihtol on February 13, 2009:

In comparing the data sheet that you sent us . . . we have the following issues . . . .

***For the following patients there is a disagreement between your data sheet and our team's analysis with respect to the presence of chondrolysis based on the primary source material we've reviewed.*** . . . Thus for these cases we really(!) need . . . all the Xrays/x-ray reports available on these cases - INCLUDING THOSE FROM OFFICES OTHER THAN THE DOCTOR'S as soon as possible so I can resolve this in the coming week.

***In some of these cases we cannot find documentation of chondrolysis. In other cases we found chondrolysis but it did not show on your sheet.*** . . . As you can see, like you, we've put a huge amount of effort into this study. ***We're very close, but because of the number of discrepancy cases the conclusion of the study will be strongly affected by the resolution of the discrepancy.*** We suspect that in many cases the issue is that your office had information not included in the doctor's records that established the diagnosis of chondrolysis. That is the missing documentation that is needed to complete the study. . . .

Exhibits in Supp. of Renewed Mot. to Strike Matsen, Ex. 4, p. 4 (emphasis added).

Message from Mr. Wihtol to Dr. Matsen on February 14, 2009:

Dr. Matsen: ***You may be using an older version of the Data Sheet from Dr. Benz. Attached is the current, and I hope final, Data Sheet.*** . . . Has your team diagnosed chondrolysis in any othe[r] patients based on your review of records and imaging studies? We continue to work on the remaining questions you have raised.

Id. Ex. 4, pp. 3-4 (emphasis added).

Message from Mr. Wihtol to Dr. Matsen on February 14, 2009:

Dr. Matsen: We emailed the LC series of records to you today. . . . The current Benz Data Sheet was attached to a subsequent email to you today. If you did not get these things, do let me know. . . .

Id. Ex. 4, p. 3 (emphasis added).

Message from Dr. Matsen to Mr. Wihtol on February 15, 2009:

I have them and have emailed them to my team [here]. . . . ***It would have been a problem had we not uncovered the omission of these critical cases. I'm thrilled that we now have a 'full deck.'***

Please look at the enclosed spreadsheet. ***It shows 24 cases where your team and mine disagree on whether there was chondrolysis. 6 of these are the plaintiff cases and we're on our way to resolving these. In the ones below, Jeff (you) found chondrolysis and my team (Rick) did not . . . . In the remaining, my team (Rick) found chondrolysis and your team (Jeff) did not . . . .***

***Of greatest concern is the first group and I'm asking whether you have documentation for the existence of chondrolysis in these cases either from the [d]octor's records or from the records of other doctors.*** If so, can you please send me the primary source material . . . that document the chondrolysis?

This [sic] few 'issues' are making it apparent why it is critical to keep a long 'arm's distance' between the two analyses. It will make the whole study much more solid. Thanks for your partnership.

Id. Ex. 4, pp. 2-3 (emphasis added).

Message from Mr. Wihtol to Dr. Matsen on February 15, 2009:

Dr. Matsen: Glad you have safely arrived [sic] and have received the LC patients series records now. ***It is beneficial to compare your teams analysis of the record review with that of Dr. Benz's team.*** It is very important that your team rely ultimately on its review to assess the records and films.

Id. Ex. 4, p. 2 (emphasis added).

Message from Mr. Wihtol to Dr. Matsen on February 15, 2009:

Dr. Matsen: ***I have attempted to correct some of the conclusions of Dr. Benz's group on the attached spreadsheet.*** My corrections are taken from the final DataSheet of Dr. Benz . . . .

Id. Ex. 2, p. 74 (emphasis added).

Message from Mr. Wihtol to Dr. Matsen on February 15, 2009:

Dr. Matsen: I think *we have now either corrected your team's understanding whether chondrolysis was diagnosed by Dr. Benz, or directed your team to where the record of diagnosis of chondrolysis is located*, except for two patients[.] *We are still working on those two*, getting records from a third party source. *Is there anything else for us to do at this time?*

Id. Ex. 2, p. 73 (emphasis added).

Message from Dr. Matsen to Mr. Wihtol on February 15, 2009:

Dear Jeff

*(best not to include Sue in these emails, please). We cannot find documentation for chondrolysis for patients D, DD, G, L, and U. If your team believes it is in the records*, please indicate where this documentation may be found in the primary source materials.

*For patients EEE, GG, KKKK, MMMM; PPP, and BZ 082 our group found evidence of chondrolysis whereas yours did not.* This is not as big an issue as the five cases above.

Again, please send us the primary source documents that substantiate the diagnosis of chondrolysis for D, DD, G, L, and U[.]

Id. Ex. 2, p. 73 (emphasis added).

Mr. Wihtol also sent several e-mails to Dr. Matsen with the following direction:

Dr. Matsen: Attached are the redacted patient plaintiff records for LC 0007. *This patient should be added to your study because Dr. Benz was the surgeon, he did arthroscopic surgery on this patient, a pain pump was used in the GH joint following the surgery, and the patient developed chondrolysis afterwards.*

Horwitz Decl. in Supp. Suppl. Mem. to Exclude Matsen, Ex. C (emphasis added).

Thus, not only did Mr. Wihtol create the idea for the 396-study, provide the raw patient data for the study, and select the nurse to perform data extraction for the study, Mr. Wihtol also compared his (or his "team's") findings from the data with those of Dr. Matsen and encouraged Dr. Matsen to do the same, identified patients who should be diagnosed with chondrolysis, conferred with Dr. Matsen to "correct" diagnoses of chondrolysis, and directed Dr. Matsen to include certain patients in the study. Contrary to plaintiffs' strenuous assertions, Mr. Wihtol was more than a "mere conduit"

for the delivery of raw data.

Putting to rest any doubt that these communications are not what they seem, Dr. Matsen conceded at his deposition that he contacted Mr. Wihtol for information and in doing so disregarded protocol intended to insulate the study from ongoing litigation. Matsen Dep. Jan. 28, 2010, pp. 423, 447, 449; see id. p. 428 (when asked if he "went to Mr. Wihtol for information about the findings," Dr. Matsen answered, "When - that's right."). Although Dr. Matsen emphasized that his team's analysis was based on only its interpretation of "primary source documents" such medical records, Dr. Matsen admitted that he compared his data analysis with that of Mr. Wihtol's "team" to discern "inconsistencies" or "discrepancies." Id. pp. 424-26, 432-33, 435, 447, 449; see also Matsen Dep. Feb. 17, 2010, p. 724. Such discrepancies were apparently "corrected" after Dr. Matsen requested and obtained additional records from Mr. Wihtol. Regardless of whether Dr. Matsen "relied" on the primary source materials in his analysis of the data, the fact remains that his analysis was affected, altered, and "corrected" by Mr. Wihtol or information obtained from him.

It is therefore unsurprising that Dr. Matsen considered Mr. Wihtol's participation "helpful" and entitled Mr. Wihtol to access information pertinent to the 396-study, even as defense counsel was denied such information on grounds that it was "proprietary." See Exhibits in Supp. of Renewed Mot. to Strike Matsen, Ex. 2, p. 53, Ex. 4, p. 26; Matsen Dep. Jan. 28, 2010, p. 450 ("I shared it with [Wihtol] because he was helping us resolve the data discrepancy."); Skocilich Decl. in Supp. of Defs.' Mot. to Exclude Matsen, Ex. F, p. 5. Dr. Matsen went so far as to say that Mr. Wihtol could be credited as an author of the study if he wished to be. Id. Matsen Dep., Jan. 28, 2010, p. 457.

Moreover, the e-mail communications that reflect Mr. Wihtol's involvement were not

produced by Mr. Wihtol or Dr. Matsen, even after plaintiffs were twice ordered to produce documents, including e-mail communications, relating to the subject matter of the 396-study. Instead, Ms. Moerer produced the documents in response to a deposition subpoena. Given that Mr. Wihtol eventually was advised by Dr. Matsen "not to include Sue on these e-mails," the court is not confident the full extent of Mr. Wihtol's involvement or his communications with Dr. Matsen have been disclosed. In any event, I find that counsel's withholding of e-mail communications clearly violate the court's discovery orders, as reflected by a cursory review of the discovery disputes involving Dr. Matsen.

On September 11, 2009, the Stryker defendants (Stryker) moved to compel the production of e-mail communications between plaintiffs' counsel and Drs. Beck and Matsen. In granting Stryker's motion, I stated the following:

***Plaintiffs shall produce e-mail communications between Dr. Beck and plaintiffs' counsel and between Dr. Matsen and plaintiffs' counsel that were reviewed or considered by Drs. Beck or Matsen in preparing their expert reports submitted in these pain pump cases. Specifically, plaintiffs shall produce all e-mail communications that request an expert opinion, respond to a request for an expert opinion, or that otherwise discuss or address the substance of the experts' reports. Should plaintiffs continue to argue that review of the e-mail communications is too burdensome, plaintiffs may submit all e-mail communications between Drs. Beck and Matsen and counsel to the court for in camera review.***

Huggins v. Stryker Corp., 07-1671-AA, doc. 210 (emphasis added).

On October 16, 2009, Magistrate Judge Coffin ordered plaintiffs to produce certain documents relevant to Dr. Matsen's study within ten days, stating: "To be clear: the scope of expert discovery in these pain pump cases extends to all documents and other ***information written, prepared, reviewed, or considered by an expert witness that pertain to the subject matter on which the expert intend[s] to testify.***" Huggins, 07-1671-AA, doc. 254, p. 7 (emphasis added). Judge

Coffin warned plaintiffs that Dr. Matsen's testimony would be stricken if they failed to comply.<sup>22</sup>

Despite clear direction from two federal judges regarding the scope of discovery, plaintiffs nonetheless withheld e-mail communications between Mr. Wihtol and Dr. Matsen that discuss the diagnosis of chondrolysis in certain patients involved in the 396-study - communications considered by Dr. Matsen that clearly discuss, address and/or pertain to the subject matter of his opinion.

Notably absent from plaintiffs' responsive briefs is any credible explanation for Mr. Wihtol's communications with Dr. Matsen or their lack of disclosure. Instead, plaintiffs gamely attempt to excuse the blatant disregard of court orders by arguing, as they have in response to almost every motion to compel filed by defendants, that the above e-mail exchanges do not address the substance of Dr. Matsen's expert report and were not relied on in the development of his opinion.<sup>23</sup> Plaintiffs' arguments regarding the content of the e-mail communications, their relevance to Dr. Matsen's opinion, and defendants' right to obtain them are without merit and warrant no further discussion.

Ultimately, the court need not rely solely on Rule 26 to exclude Dr. Matsen's expert testimony, when the circumstances of the 396-study and its unfinished status render Dr. Matsen's opinion irreparably tainted by litigation bias and unreliable. At best, Dr. Matsen sought "clarification" from Mr. Wihtol concerning his analysis of the patient data. At worst, Mr. Wihtol

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<sup>22</sup>These orders followed several other rulings ordering production of documents relevant to the expert opinions of Drs. Beck, Swanson, and Matsen - orders that clearly identified the scope of expert discovery in these cases. Counsel's repeated refusal to abide by the court's discovery orders is mystifying and ultimately counterproductive to their stated goal of moving these cases forward. Had plaintiffs produced the documents requested in a timely manner, the *Daubert* proceeding would have been completed in November, if not October.

<sup>23</sup>Plaintiffs also argue in earnest that Ms. Moerer was not involved in data analysis, and had no inappropriate communications with Mr. Wihtol. Plaintiffs also argue that her e-mail communications bolster their assertion that the study was conducted at arms length from counsel. However, at issue are Mr. Wihtol's communications with Dr. Matsen, not Ms. Moerer's.

utilized Dr. Matsen in an orchestrated attempt to design, conduct, and complete a research study for the purpose of supporting litigation in which he has a vested economic interest. Either way, the resulting litigation bias, combined with the ever-changing and still unfinished report that is the crux of Dr. Matsen's opinion, render his testimony unreliable and inadmissible.<sup>24</sup>

## 2. Dr. Charles Beck

Dr. Beck is a board-certified orthopedic surgeon who has practiced in Salt Lake City, Utah for over twenty years. Dr. Beck obtained his medical degree from Louisiana State University and completed an orthopedic residency in New Orleans and fellowship training in orthopedic surgery and sports medicine in Salt Lake City. Beginning in the 1990s, Dr. Beck was the team physician to the U.S. Snowboard Team for almost ten years, and he continues to serve as a consultant for the U.S. Ski Team. In this litigation, Dr. Beck has rendered the opinion that continuous infusion can cause chondrolysis, based on his review and analysis of patients records in the Hansen/Beck Study, review of additional medical literature, and his training, knowledge, and experience. Beck Expert Report, pp. 3-5.

Defendants first argue that Dr. Beck's opinion lacks indicia of reliability because it differs from the conclusions of his published study. Defendants emphasize that the Hansen/Beck Study suggests merely an "association" between continuous infusion and chondrolysis, while Dr. Beck's expert opinion concludes that continuous infusion is a scientifically valid and plausible cause of chondrolysis. Thus, defendants argue that Dr. Beck's expert opinion is at odds with the scientific literature he authored.

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<sup>24</sup>Other experts who considered and reviewed the 396-study likewise cannot rely on it as support for their opinions.



I find a distinction between the purpose of the Hansen/Beck Study and the opinions Dr. Beck has reached as an expert. The purpose of the Hansen/Beck Study was to present information about patients who developed chondrolysis after receiving continuous infusion via pain pumps; it was not intended as a review of all relevant information to ascertain causes of chondrolysis. Beck *Grossnickle* testimony, Mar. 3, 2009, Vol. 5B, p. 1225. Dr. Beck's opinion, on the other hand, is based on his personal experience and training as a surgeon, his review and participation in the Hansen/Beck Study, and review of relevant medical literature. To the extent any inconsistency exists, it is an appropriate avenue for cross-examination.

Second, defendants assert that Dr. Beck's opinion, as opposed to the Hansen/Beck Study, has not been subjected to peer review, lacks general acceptance in the medical community, and is not supported by conclusive epidemiological or medical evidence of causation. None of these factors warrants exclusion of Dr. Beck's testimony. W.R. Grace, 504 F.3d at 765 (epidemiological evidence is not necessary to prove causation); Norris, 397 F.3d at 882 ("In cases where there is no epidemiology challenging causation available, epidemiological evidence would not necessarily be required."); Clausen, 339 F.3d at 1056 (even if an expert's research is not "subjected to normal scientific scrutiny through peer review and publication," the "proffer of scientific testimony may still be deemed reliable enough to be admitted"); Domingo, 289 F.3d at 605 ("*Daubert* does not require that every aspect of a theory of medical causation be supported by research on the identical point[.]"); Kennedy, 161 F.3d at 1229 (the lack of an established "cause-effect relationship" does not render expert testimony inadmissible).

Third, defendants argue that the cited medical literature does not lend support to Dr. Beck's testimony. Joiner, 522 U.S. at 146; Domingo, 289 F.3d at 606-07. Defendants emphasize that Dr.

Beck's opinion rests on nothing more than the Hansen/Beck Study, a case series that does not rise to the level of scientific reliability required by *Daubert*, and in vitro and animals studies that cannot reliably be extrapolated to human articular cartilage. I find these sources sufficient to support Dr. Beck's opinion.

Dr. Beck relies on the whole of medical evidence that includes case series associating continuous infusion and chondrolysis and in vitro and animal studies demonstrating that local anesthetics have a toxic effect on cartilage cells. Beck Dep., Aug. 31, 2009, p. 538.<sup>25</sup> Dr. Beck thus bases his opinion on "objective, verifiable evidence" that is within "the knowledge and experience of the relevant discipline." Primiano, 2010 WL 1660303, at \*5 (quoting Sandoval-Mendoza, 472 F.3d at 654); see also Kennedy, 161 F.3d at 1228. Further, Dr. Beck's study of patients who developed chondrolysis after receiving continuous infusion, combined with his review of peer-reviewed medical literature and experience as an orthopedic surgeon, "is the ordinary methodology of evidence based medicine." Primiano, 2010 WL 1660303, at \*6. Therefore, any perceived weakness in Dr. Beck's methodology goes to weight rather than admissibility.<sup>26</sup>

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<sup>25</sup>Defendants contend that Dr. Beck fails to reconcile his study and opinion with Gobezie's 2006 study that analyzed complications of more than 600 arthroscopies involving pain pumps infused with local anesthetics, with no mention of chondrolysis. However, Gobezie is a one-page abstract discussing complications such as breakage of the pain pump catheter. It is unclear whether the study was designed to detect longer-term complications. Gobezie et. al, *Complications Associated with the Use of Pain Control Infusion Pumps (PCIPs) After Arthroscopic Shoulder Surgery - Poster Presentation* (June 2006). Regardless, Dr. Beck's failure to reconcile Gobezie is not grounds for exclusion.

<sup>26</sup>In their supplemental memorandum, defendants also contend that Dr. Beck chose arbitrary start and end dates for the Hansen/Beck Study, has no documentation that all patients in the study received continuous infusion intra-articularly, and failed to disclose records of two patients in the study. Dr. Beck explained the reasons for the study's parameters and for not producing the two patient records. Beck Dep. Jan. 26, 2010, pp. 687-88, 790-92. I find these topics appropriate for cross-examination rather than exclusion.

Finally, defendants argue that plaintiffs' counsel Mr. Wihtol drafted Dr. Beck's expert report in contradiction of the requirements of Rule 26. Given the evidence presented, it cannot be disputed that Mr. Wihtol authored the report, while Dr. Beck reviewed and edited it. In fact, Dr. Beck informed Mr. Wihtol that part of the report sounded more like "an attorney making his case than a doctor giving his opinion," and that the language should be "toned down" to avoid the appearance of putting "words in [his] mouth." Horwitz Decl. in Supp. Mot. to Exclude Beck, Ex. H.

While I recognize the realities of litigation often necessitate counsel's assistance in the preparation of expert reports, the extent of Mr. Wihtol's role in drafting Dr. Beck's expert report approaches the outer limits of acceptable assistance. Nevertheless, I do not exclude Dr. Beck's testimony on this ground. Importantly, Dr. Beck conducted his study and formulated his opinion prior to his retention as an expert. Further, through his deposition testimony, Dr. Beck adopted the substance of his report and explained the basis for his opinion. Trigon Ins. Co., 204 F.R.D. 277 at 294; cf. In Re Jackson Nat'l Life Ins. Co. Premium Litig., 2000 WL 33654070, at \*2 (W.D. Mich. Feb. 8, 2000) (finding that an expert deposition, "rather than affording opportunity to remedy any prejudice actually compounded the violation"). Thus, counsel's involvement does not warrant exclusion of Dr. Beck's testimony, though "it may undermine its weight and credibility." Mack v. AmerisourceBergen Drug Corp., 671 F. Supp. 2d 706, 712 (D. Md. 2009).<sup>27</sup>

In sum, I find Dr. Beck's opinion on general causation reliable under the threshold requirements of Rule 702 and *Daubert*, and it will be admitted at trial.<sup>28</sup>

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<sup>27</sup>For the same reasons, I reject this argument as it pertains to Dr. Basamania.

<sup>28</sup>Defendants also move to strike the testimony of Dr. Beck, along with that of Drs. Badylak and Basamania, regarding the applicable standard of care for pain pump manufacturers and relevant FDA labeling requirements. Their expert reports discuss what pain pump manufacturers

### 3. Dr. Basamania

Dr. Basamania is a orthopedic surgeon who specializes in shoulder surgery and, according to plaintiffs, has performed thousands of shoulder surgeries during his 35-year career. Before pursuing a private practice in Seattle, Washington, Dr. Basamania spent ten years on the medical faculty at Duke University. In support of his expert opinion that continuous infusion can cause chondrolysis, Dr. Basamania cites his review of relevant medical literature, including the Hansen/Beck Study, and his review of patient charts culminating in a 2006 presentation linking continuous infusion to glenohumeral chondrolysis. Basamania Expert Report, pp. 2-4.

As with most of plaintiffs' experts, defendants argue that Dr. Basamania's opinion is merely an untested and unproven hypothesis that cannot reliably support causation. Defendants discount Dr. Basamania's reliance on the Hansen/Beck Study and other medical literature, given the ultimate conclusions that the cause and etiology of chondrolysis remains "unknown." Defendants also argue that Dr. Basamania's 2006 presentation regarding chondrolysis is an unreliable source for his opinion, because it is based on a last-minute revelation rather than scientific research. Alternatively, defendants move to strike Dr. Basamania's testimony based on the failure to disclose the patient

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"should have" known about the risks of continuous infusion, the duty of care pain pump manufacturers should exercise with respect to the testing, promotion, and sale of pain pumps, and the FDA requirements for approval of arthroscopic uses. Defendants argue that Drs. Beck, Badylak, and Basamania are patently unqualified to render "expert" opinions on FDA regulations or requirements and cannot establish legal duties under the "guise" of expert opinion or industry practice. Plaintiffs did not respond to these arguments given the parties' agreement to limit the motions to general causation. Regardless, I agree that such testimony, as set forth in the expert reports, should not be allowed. Drs. Beck, Badylak, and Basamania admittedly have limited, if any, FDA regulatory experience, and the proper duty of care exercised by a "prudent, careful" pain pump manufacturer is beyond the scope of their expertise. Badylak Dep., June 13, 2009, pp. 26-27; Beck Dep., Aug. 21, 2009, p. 236. That said, I will allow testimony as to their experiences with pain pump labeling and the like, if based on their personal knowledge and experience.

records reviewed as part of his 2006 presentation.

As discussed above, *Daubert* does not require conclusive and definitive evidence of causation to deem an expert's opinion reliable, and Dr. Basamania's opinion will not be excluded on such grounds. Westberry, 178 F.3d at 262; Kennedy, 161 F.3d at 1229-30; In re Ephedra, 393 F. Supp. 2d at 191. Further, Dr. Basamania's reliance of case studies such as the Hansen/Beck study adequately supports his opinion when considered with the medical literature demonstrating the chondrotoxicity of bupivacaine and his knowledge and experience as a surgeon. However, I agree with defendants that Dr. Basamania cannot rely on his review of patient charts underlying his 2006 presentation and grant their motion to strike to that extent.

As set forth in his expert report, until two days before his presentation, Dr. Basamania believed that "use of excessive thermal inside the joint during surgery" caused chondrolysis in the patients studied. Basamania Expert Report, p. 3. After discovering that a thermal device was not used in one procedure, Dr. Basamania began "to panic," because he thought he would be unable to explain why that patient developed chondrolysis. Id. ("If she did not have any thermal used, then we could not blame the thermal."). Dr. Basamania again reviewed the records and realized that intra-articular continuous infusion via pain pump was a common factor in all of the procedures. Dr. Basamania then "did a drastic change to all the slides for the presentation," and "completely change[d] the presentation from suggesting [chondrolysis] was caused by thermal, to concluding the pain pumps had caused the chondrolysis." Id.

Other than the common presence of pain pumps and continuous infusion, Dr. Basamania provides no explanation for his sudden change of opinion regarding the cause of chondrolysis or why he ruled out thermal devices as a potential cause. See Turner, 229 F.3d at 1208 (excluding opinion

that was developed “more as an after thought, in an ad hoc manner”). More importantly, defendants are severely hampered in challenging Dr. Basamania's opinion because plaintiffs have not produced the patients records reviewed by Dr. Basamania in conjunction with his 2006 presentation.

Plaintiffs respond that Dr. Basamania cannot produce the medical records in question, because he does not possess them and can no longer obtain them from Duke University. Plaintiffs maintain that Dr. Basamania's testimony should not be excluded for failing to disclose what he does not possess. Plaintiffs also make the rather curious argument that the expert disclosure requirements of Rule 26(a)(2)(B) apply only to material reviewed by an expert *after* being retained in that capacity. Plaintiffs provide no persuasive authority for their novel interpretation of the expert discovery rule, and I find their argument inconsistent with its purpose.

Rule 26 and relevant caselaw make clear that an expert must disclose and produce the "data or other information considered by the expert in forming the opinions" to be given at trial. Fed. R. Civ. P. 26(a)(2)(B); Nguyen v. IBP, Inc., 162 F.R.D. 675, 681 (D. Kan. 1995). Here, Dr. Basamania clearly "considered" the patient charts in forming his opinion; they not only led to a change in his presentation, they constitute the primary basis of his opinion.

Given that Dr. Basamania will not or cannot comply with the disclosure requirements of Rule 26, the court must decide whether and to what extent Dr. Basamania's testimony is permitted. A party who fails to disclose information required by Rule 26(a) cannot offer testimony based on such information unless "substantial justification" exists for the failure and it is "harmless." Fed. R. Civ. P. 37(c)(1). I find the failure to disclose neither substantially justified nor harmless.

Plaintiffs provide no record of any attempts by them or Dr. Basamania to obtain the relevant patient charts from Duke University or from another source with access to the records. Instead,

plaintiffs complain that defendants could have and should have requested the records from the patients' surgeon. However, it is not defendants' responsibility to track down documents that purportedly support the opinion of plaintiffs' expert; it is plaintiffs duty to disclose the relevant documents or accept the consequences for failing to do so. Moreover, it is questionable whether defendants possess the relevant identifying information to request specific patient charts from a third-party physician. Regardless, given plaintiffs' apparent lack of effort to obtain the patient charts underlying Dr. Basamania's 2006 presentation, I do not find the failure to disclose them substantially justified.

Further, the failure is not harmless. Contrary to plaintiffs' arguments, the patient records do not constitute information relevant to Dr. Basamania's general background or experience as a orthopedic surgeon. Rather, these patient charts were the driving force behind Dr. Basamania's determination that continuous infusion can cause chondrolysis and are critical to his expert opinion. Absent production of the records, defendants are precluded from meaningful cross-examination of Dr. Basamania or challenging his causation opinion. At a minimum, Rules 26 and 37 require exclusion of Dr. Basamania's opinion testimony as it relates to the patient charts or his presentation. Accordingly, Dr. Basamania cannot reference or rely on his 2006 presentation in rendering his opinion at trial.

#### 4. Dr. Badylak

Dr. Badylak is a full professor in the Departments of Surgery and Bioengineering at the University of Pittsburgh and is the Deputy Director of the McGowan Institute for Regenerative Medicine and the Director of the Center for Preclinical Studies. Dr. Badylak obtained his medical degree from Indiana University. Prior to that, he obtained a D.V.M., a M.S. in Clinical Pathology,

and a PhD in Anatomic Pathology from Purdue University. From 1985 to 2001, Dr. Badylak was the head team physician for Purdue University. Since 1985, Dr. Badylak has conducted research in the field of tissue engineering and regenerative medicine, which is "the study of diseased or missing tissues and the development of strategies and methodologies for the reconstruction or regeneration of such tissues." Badylak Expert Report, p. 1. Dr. Badylak holds more than 50 patents in the field of regenerative medicine, including patents relating to technology for the treatment of shoulder pathology. Id. In his expert report, Dr. Badylak opines that the intra-articular use of pain pumps with local anesthetics is the primary cause of plaintiffs' chondrolysis.

Defendants argue that Dr. Badylak impermissibly extrapolates facts from the medical literature to espouse an untested causation theory based on the turnover rate of synovial fluid, and fills the notable "gaps" in his methodology by relying on the "whole" of the medical evidence. Defendants emphasize that Dr. Badylak is not an orthopedic surgeon, has never performed shoulder surgery, and has never diagnosed or treated a patient with glenohumeral chondrolysis.

Dr. Badylak describes his causation theory as follows:

The likely mechanism by which chondrolysis is caused . . . is by decreasing the turnover rate of synovial fluid [in the shoulder joint] as a consequence of the vasoconstriction to the blood vessels that supply the lining cells of the joint capsule (synoviocytes). By decreasing the blood supply and thus decreasing the turnover rate of synovial fluid, the high concentration of the primary chondrotoxin . . . remains in direct contact with the articular surface for a longer period of time causing progressive death of the articular surface cartilage cells.

Badylak Expert Report, p. 2; see also Greis, p. 1343 (intra-articular pain pump placement "likely exposes the cartilage to a higher volume and concentration of bupivacaine . . . and the concentration may be sufficient to damage the cartilage"). Dr. Badylak also asserts that the "destructive effect" of the pharmacologic agents "becomes worse with increasing time and/or increasing dose of the drug



in contact with the cartilage cells." Badylak Expert Report, p. 2.

In support of his opinion, Dr. Badylak relies on independently reliable evidence that continuous infusion causes harm to articular cartilage, as established in both Chu studies, the Dragoo study, Gomoll I, and the Karpie study, along with various case series. See Badylak Expert Report, Ex. A. Dr. Badylak further explains how the whole of medical literature informs his opinion:

If you look at this article by Busfield, obviously you cannot come to the conclusion that intra-articular infusion of Marcaine with these pain pumps causes chondrolysis. . . . You combine his article with the Hansen and Beck report, now the story starts to get a little bit more complete. You combine that with Constance Chu's basic science showing that the medication that's being delivered into the joint kills chondrocytes, the story becomes even more compelling. You add a pre-clinical study from Gomoll that shows when you deliver [anesthetics] intra-articularly in the shoulder joint of a predictive pre-clinical model and you get the problem. I mean, it becomes an avalanche.

Badylak Dep., July 13, 2009, p. 154, 171, 176; see also Badylak Dep., July 27, 2009, pp. 325-26 ("You combine [the Hansen/Beck Study] with the other experiences, the in vitro data, the pre-clinical studies and so forth . . . this becomes a no-brainer, frankly.").

Although he has no surgical experience, Dr. Badylak calls upon his extensive knowledge and experience with damaged tissue, and when combined with review of medical literature, his methodology is of a kind that physicians routinely employ in the course of the profession. Primiano, 2010 WL 1660303, at \*6 ("[P]hysicians must use their knowledge and experience as a basis for weighing known factors along with the inevitable uncertainties to mak[e] a sound judgment."); Heller, 167 F.3d at 155. To the extent Dr. Badylak extrapolates from the medical research, defendants' arguments go to the weight rather than the admissibility of his testimony.

Accordingly, Dr. Badylak's opinion is founded on reliable methodology and sufficient facts, and it will be admitted.

### 5. Dr. Dragoo

Dr. Jason Dragoo is an Assistant Professor of Orthopedic surgery at Stanford University School of Medicine, Sports Medicine. Dr. Dragoo is the head team physician for Stanford University's athletic programs and a physician for the U.S. Ski Team. Dr. Dragoo performs research on the restoration of articular cartilage and runs a full-time laboratory. Specifically, Dr. Dragoo's "research interests are in functional restoration of cartilage . . . and the mechanisms of cartilage degeneration including the use of local anesthetics." Dragoo Expert Report, p. 1. As an expert in this litigation, Dr. Dragoo renders the opinion that continuous infusion can cause "cartilage degeneration in a dose-duration dependent manner." Dragoo Expert Report, p. 7. In support of his opinion, Dr. Dragoo relies on his own study, the Chu and Gomoll studies, case series, and other relevant medical literature. *Id.* pp. 6-7; Dragoo Dep., June 12, 2009, pp. 67-68.

Dr. Dragoo devised a study that exposed human chondrocytes to certain pH levels of bupivacaine. Dr. Dragoo created a model that allowed the constant flow of fluid to the cartilage cultures to "mimick[] [the] metabolism of medication which would be applied to the shoulder through a pain pump." Dragoo Expert Report, p. 5. Dr. Dragoo found that increased exposure, either through higher dosages or longer periods of exposure, caused chondrotoxicity.

The results of the trial showed that any local anesthetic preparation containing epinephrine showed a significant decrease in chondrocyte viability at all times points. At 72 hours, pumps containing 0.5% bupivacaine without epinephrine also showed significant loss of chondrocyte viability. Follow-up studies . . . showed no loss of cell viability when the cells were cultured with epinephrine alone, however, when the cell cultures were titrated to the pH of the meds containing epinephrine there was a significant loss of chondrocyte viability. . . . Therefore, we concluded that the chondrotoxic effects of local anesthetics containing epinephrine are likely due to both pH and the preservative sodium metabisulfate.

Dragoo Expert Report, pp. 5-6. Given this study and his review of other literature, Dr. Dragoo

opines that local anesthetics infused via pain pump may be chondrotoxic when infused for less than 48 hours and are likely chondrotoxic when infused for greater than 48 hours.

Defendants assert their stock arguments that Dr. Dragoo's opinion is merely an unreliable hypothesis without peer-review, general acceptance, or support in the medical literature, because no evidence establishes a direct and conclusive link between continuous infusion and chondrolysis. These arguments are rejected for the reasons explained above. Defendants also maintain that Dr. Dragoo fails to explain the contradictory findings in Gomoll II regarding cartilage regeneration in rabbits shoulder joints three months after exposure to local anesthetics. However, Dr. Dragoo addressed Gomoll II and explained that rabbits can regenerate cartilage defects while humans cannot. Dragoo Dep., June 12, 2009, pp. 207-08, 228.

Moreover, Dr. Dragoo fully explained the reasoning and methodology of his opinion, as supported by his study and that of others:

My testimony is that the chondrocytes can be damaged with certain dose dependent administration of local anesthetics. And then if those chondrocytes are damaged, then it is medically reasonable, especially considering the other literature as a whole, including the clinical literature, that [such chondrocyte damage] would be a causative factor in the development of chondrolysis in that particular patient.

Id. pp. 135-36, 172; see also id. p. 49 ("If you were to ask my professional opinion, is the chondrocyte loss that we've established in our study, is that medically probable that this cartilage loss would lead to chondrolysis, I would have to say yes."). Dr. Dragoo further explained how cartilage damage, chondrocyte death, and the cell changes that he and others have observed relate to the disease of chondrolysis. Id. at 136, 172. Notably, Dr. Dragoo has extensive knowledge and experience in the area of cartilage degeneration and restoration, lending further credence to his methodology. Primiano, 2010 WL 1660303, at \*6.

Thus, even if Dr. Dragoo cannot explain "the entire link, the entire path or the stops that are involved with chondrolysis," Dragoo Dep., June 12, 2009, p. 202, his opinion and testimony is "sufficiently compelling proof that the agent must have caused the damage *somehow*." Daubert II, 43 F.3d at 1314. Accordingly, Dr. Dragoo's testimony will be admitted at trial.

#### 6. Dr. Swanson

Dr. John Swanson is a board-certified orthopedic surgeon. Dr. Swanson obtained his medical degree from the University of Iowa in 1979 and completed an internship at Harborview Medical Center in Seattle, Washington. After completing an orthopedic surgery residency, Dr. Swanson pursued a private practice in orthopedic surgery and performed numerous orthopedic shoulder surgeries. Since 2001, Dr. Swanson has practiced occupational orthopedics and conducts independent medical examinations and reviews medical records as an independent contractor.

Dr. Swanson initially observed shoulder chondrolysis in late 2005 and early 2006 when conducting independent medical examinations of approximately ten patients in workers compensation cases. Based on these examinations, his review of medical records involving chondrolysis patients, and review of relevant medical literature, Dr. Swanson concludes that the intra-articular use of pain pumps to administer local anesthetics can cause glenohumeral chondrolysis. In his report, Dr. Swanson cites the Hansen/Beck Study, and the Chu, Dragoo, and Gomoll studies, among others, in support of his opinion. Swanson Expert Report, pp. 5-10.

Defendants again assert the arguments that Dr. Swanson's opinion lacks peer-review, general acceptance in the medical community, or factual support from the medical literature. Given the court's discussion above and the state of the medical literature, defendants' arguments are not well-taken. Primiano, 2010 WL 1660303, at \*6; Kennedy, 161 F.3d at 1229-30; Daubert II, 43 F.3d at

1314, 1318-19; In re Ephedra, 393 F. Supp. 2d at 189-90; In re PPA, 289 F. Supp. 2d at 1242.

Defendants also take issue with Dr. Swanson's epidemiology analysis of the Hansen/Beck Study and application of the Bradford Hill criteria.<sup>29</sup> After attending an epidemiological methods conference, Dr. Swanson concluded that the Hansen/Beck Study was similar to a cohort study because of the two identified patient populations. Dr. Swanson then performed his own epidemiological assessment of the Hansen/Beck data. Swanson Dep., Sept. 4, 2009, p. 321. Defendants strenuously argue that Dr. Swanson cannot provide a reliable epidemiological analysis of the Hansen/Beck Study based on his brief participation at a conference. I am inclined to agree and find that Dr. Swanson is not particularly qualified to render an opinion based on application of the Bradford Hill criteria to the Hansen/Beck Study, as such analysis is epidemiological in nature. In re Fosamax, 645 F. Supp. 2d at 188; REFERENCE MANUAL, pp. 374-79. Regardless, plaintiffs assert that Dr. Swanson does not intend to testify regarding his supplemental analysis of the Hansen/Beck Study.

Aside from Dr. Swanson's utilization of epidemiology and the Bradford Hill criteria, defendants' challenges go to the weight rather than the admissibility of Dr. Swanson's opinion, and his testimony will be admitted.

#### 7. Dr. Trippel

Dr. Stephen Trippel is a board-certified orthopedic surgeon and a full professor of orthopedic

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<sup>29</sup>Nine factors are generally employed by researchers when determining whether an association reflects a true cause-effect relationship. REFERENCE MANUAL, p. 375. They include: 1) temporal relationship; 2) strength of association; 3) dose-response relationship; 4) replication of results; 5) biological plausibility of association; 6) consideration of alternative explanations; 7) cessation of exposure; 8) specificity of association; and 9) consistency with other relevant knowledge. Id. pp. 376-79. These factors are commonly known as the Bradford Hill factors, in recognition of A. Bradford Hill's contributions and expansion of the criteria. Id. 376.

surgery at Indiana University Medical School, where he conducts research on cartilage tissue. Previously, Dr. Trippel was on the faculty at Harvard Medical School and Chair of Orthopedic Surgery at Indiana University Medical School.

Dr. Trippel's expert report concludes that continuous infusion is a probable and likely cause of chondrolysis. Consistent with the opinions of Drs. Badylak and Dragoo, Dr. Trippel believes that infusion of local anesthetics displaces the synovial fluid that provides nutrients to cartilage cells, and the increased and prolonged exposure to anesthetics causes mortality and the irreversible loss of cartilage tissue. Trippel Expert Report, pp. 6-7; Trippel Dep. Aug. 28, 2009, pp. 107-08. Dr. Trippel relies on his education, training, and experience as an orthopedic surgeon and as a researcher of cartilage tissue, as well as his review of the literature and medical research. Dr. Trippel discusses numerous studies, including the Chu, Dragoo, Gomoll, and Greis studies, and the Hansen/Beck Study. Trippel Expert Report, pp. 14-23.

Defendants take issue with Dr. Trippel's reference to the differential diagnosis methodology when discussing general causation. Trippel Expert Report, p. 14. Defendants contend that Dr. Trippel impermissibly "rules in" continuous infusion as a cause of chondrolysis without evidence of an established causal link. Defendants also argue that Dr. Trippel did not reliably "rule out" other causes of chondrolysis, as he admitted that it is "multi-factorial."

For the reasons explained above, I find that the evidence demonstrating chondrotoxicity after prolonged exposure to bupivacaine, along with the noted temporal relationship between continuous infusion and chondrolysis and the nature of the disease, provide an adequate basis for Dr. Trippel to utilize the differential diagnosis method in rendering an opinion on general causation. Best, 563 F.3d at 178-79; Westberry, 178 F.3d at 262; Kennedy, 161 F.3d at 1229-30; In re Fosamax, 645 F.

Supp. 2d at 178-79. While Dr. Trippel recognized other potential causes of chondrolysis, he also noted the reported occurrences of chondrolysis with continuous infusion as an isolated or common factor.

Finally, Dr. Trippel sufficiently explains his theory that continuous infusion displaces synovial fluid and, through the increased and prolonged exposure to local anesthetics, destroys cartilage cells:

The shoulder joint is an enclosed space, and under normal conditions, it's occupied by synovial fluid. If additional fluid is introduc[ed] into that enclosed space, then the first thing that will happen is that the synovial fluid that currently occupies it will become diluted by that material. The synovial lining is a dynamic entity and serves as a filter for the joint, so that eventually the materials that are in the joint space will be taken out, and if the production of new synovial fluid, which is relatively slow, is exceeded by the rate of influx of foreign solutions, which is relatively fast, then the term "displaced" becomes more appropriate than diluted.

Trippel Dep., Aug. 28, 2009, pp. 107-08. Dr. Trippel also explained that he would expect no current studies on the displacement of synovial fluid, "because they'd say it's obvious." Id. at 113-14.

Defendants nonetheless emphasize that Dr. Trippel cannot identify the precise dose, duration, or concentration of anesthetic that would cause displacement of synovial fluid, its volume or turnover rate, or the "uptake" rate of medication. Id. at 109-10, 113. However, "precise information concerning the exposure necessary to cause specific harm to humans and exact details pertaining to the plaintiff's exposure . . . need not invariably provide the basis for an expert's opinion on causation." Westberry, 178 F.3d at 264; see also Domingo, 289 F.3d at 605-06; Daubert II, 43 F.3d at 1314, 1318-19.

Moreover, Dr. Trippel's extensive experience as a researcher of cartilage tissue combined with his review of the medical literature provides a sufficient basis for his displacement theory.

Primiano, 2010 WL 1660303, at \*4, 6; REFERENCE MANUAL, pp. 470-71.<sup>30</sup> Therefore, his testimony meets *Daubert's* reliability threshold, and it will be admitted.

#### 8. Drs. Greenland and Wells

Dr. Sander Greenland is an epidemiologist and Dr. Martin Wells is a biostatistician, both with extensive and impressive credentials. Dr. Greenland obtained a Master's Degree in mathematics from the University of California, Berkeley, and a doctorate in public health from University of California, Los Angeles (UCLA). Dr. Greenland is a full professor of Epidemiology and Statistics at UCLA, where he has taught epidemiology and statistics since 1979. Dr. Greenland is the author and editor of the leading textbook for courses in advanced epidemiology, and has published more than 300 papers in peer-reviewed literature. Dr. Wells is the Chair of the Department of Statistical Sciences at Cornell University, where he served for six years as Chair of the Department of Biological Statistics and Computational Biology. Dr. Wells is also Professor of Social Statistics, Professor of Clinical Epidemiology and Health Services Research at the Cornell Weill Medical School, and Director of Research at Cornell's School of Industrial and Labor Relations. Dr. Wells has also published extensively. Given their notable accomplishments, it is unsurprising that plaintiffs retained Drs. Greenland and Wells to lend epidemiological strength to the Hansen/Beck Study.<sup>31</sup>

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<sup>30</sup>Defendants also object to Dr. Trippel's stated opinion that pain pump manufacturers did not adequately test pain pumps for intra-articular use, and that they should have known of the risks associated with continuous infusion. Trippel Expert Report, pp. 4-5, 7-9, 10-12, 14, 24. I agree that Dr. Trippel is unqualified to testify about the adequate testing of pain pumps, particularly when the adequacy of pain pump testing was information provided to him by plaintiffs' counsel. See Trippel Dep. Aug. 28, 2009, p. 176.

<sup>31</sup>Plaintiffs also retained Drs. Greenland and Wells to analyze the findings of Dr. Matsen's study. Given the court's conclusion that Dr. Matsen's testimony fails to meet the *Daubert* reliability threshold, the statistical analysis of his study is largely moot. For the record, I note that Drs. Greenland and Wells performed their initial analysis of the Matsen data based on Dr.



According to Drs. Greenland and Wells, the Hansen/Beck Study contains data sufficient for a retrospective cohort, because it compares two populations: patients who were exposed to continuous infusion and patients who were not. Greenland Expert Report, pp. 5-6, 13; Declaration of Martin T. Wells Ph.D (Wells Expert Report), p. 3; REFERENCE MANUAL, pp. 340-41. Based on Dr. Beck's finding that 12 out of 19 shoulder surgeries with continuous infusion resulted in chondrolysis, Drs. Greenland and Wells find a high association between continuous infusion and chondrolysis that cannot be attributed to chance. Greenland Expert Report, p. 8; Wells Expert Report, p. 2.

Defendants challenge the analysis of the Hansen/Beck Study as a retrospective cohort study, emphasizing that Dr. Beck did not implement controls for bias or error as is typical of cohort studies. REFERENCE MANUAL, pp. 340-41, 364, 371.

As noted above, Drs. Greenland and Wells did not review the underlying data, and their analyses do not account for the lack of controls to minimize bias. Greenland Dep. Sept. 24, 2009, pp. 166-68; Wells Dep. Oct. 5, 2009, pp. 19, 41, 120-21. Additionally, both Drs. Greenland and Wells acknowledged the limitations of the Hansen/Beck Study and their interpretation of the data. For example, Dr. Wells admitted that the numbers reported in the Hansen/Beck Study "did not add up" and that he could not ultimately determine the source of the discrepancy. Wells Dep., Oct. 5, 2009, pp. 89-91. Dr. Wells also conceded that his analysis did not account for other causal factors, though he believed it to be "an important piece of information." Id. at 133.

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Matsen's testimony in a state court trial in early 2009 and supplemented their expert reports based on a draft paper of the 396-study. See Greenland Suppl. Report, p. 3; Wells Suppl. Decl., p. 2. Given Dr. Matsen's statement that the numbers of the 396-study are likely to change, it is not a stretch for the court to find unreliable or irrelevant statistical analyses of incorrect or incomplete data.

Similarly, Dr. Greenland acknowledged that the causal inference between continuous infusion and chondrolysis was "limited" to the patients in the Hansen/Beck Study and that he "was not commenting on the general populations of shoulder arthroscopies." Greenland Dep. Sept. 24, 2009, p. 275. Dr. Greenland agreed that the Hansen/Beck Study had no controls for selection bias or confounding factors, and it did not include comparative data for unexposed patients to discern other potential causes of chondrolysis. While Dr. Greenland opines that the Hansen/Beck Study shows an association between continuous infusion and chondrolysis, he cannot identify what about it - the anesthetic, the catheter, or surgical technique - is a causal factor. *Id.* pp. 303, 322-23.

I do not find that Dr. Greenland or Dr. Wells employed unreliable methodologies in their assessment of the Hansen/Beck Study. Each analyzed the data presented to them and rendered seemingly accurate epidemiological and statistical analyses. Neither extrapolates his findings to a broader population and instead limits the analysis to the patients included in the Hansen/Beck Study. Further, Dr. Greenland testified that it was not uncommon to analyze such limited data, though he recognized that a publishable article would require "more work" and "caution." Transcript of Proceedings, Nov. 18, 2009, p. 202; Greenland Dep. Sept. 24, 2009, p. 297.

That said, I do not find the testimony of Drs. Greenland or Wells to be particularly relevant or helpful, given their inability to generalize the stated association beyond the patients involved in the Hansen/Beck Study. The limited relevance of their testimony is reflected by the following colloquy between the court and Dr. Greenland during the first *Daubert* hearing:

THE COURT: And so essentially the data in the study in Beck/Hansen is worth, really, in your opinion the conclusion that there is an extremely strong association with the use of the pain pump in these shoulder surgeries that were counted by Beck and Hansen?

THE WITNESS: Yes.

THE COURT: And that's just, in essence, all you really can draw from that data and from what is in the paper because you have not seen the underlying data, correct?

THE WITNESS: That's correct.

THE COURT: And you can't generalize it to a larger population, correct?

THE WITNESS: Yes. That's outside my expertise, for one thing.

THE COURT: Right. And you wouldn't professionally do that?

THE WITNESS: That's correct.

Transcript of Proceedings, Nov. 18, 2009, pp. 260-61; see also id. at 195. Absent generalization, the most relevant and helpful aspect of their opinions is the assertion that the association found in the Hansen/Beck Study cannot be attributed to chance.

At the same time, Dr. Greenland testified:

[T]he strength of this association is so much that it's far beyond the usual subtleties that we have to deal with in epidemiology. This is -- this is on the level of common sense. And it was taught to me when I was a student that a classic epidemiology, like an outbreak when you see these enormous associations, is a good measure of common sense, and you have to look at this kind of level of association and say -- you don't have to be -- have to have a PhD in epidemiology or anything to say -- to ask yourself would I want this procedure done to me.

Transcript of Proceedings, Nov. 18, 2009, p. 187. In other words, the degree of association between continuous infusion and chondrolysis reflected in the Hansen/Beck Study is so high that expert analysis is not necessary to infer a causal connection - it is "common sense." It is well established that "expert testimony is not helpful if it simply addresses 'lay matters which the jury is capable of understanding and deciding without the expert's help.'" In re Fosamax, 645 F. Supp. 2d at 173

(quoting United States v. Lumpkin, 192 F.3d 280, 289 (2d Cir. 1999)). Thus, Dr. Greenland's expert testimony is not necessary to "assist the trier of fact to understand the evidence or to determine a fact in issue." Fed. R. Evid. 702.

Moreover, if the court admitted the testimony of Drs. Greenland and Wells, a mini-trial would ensue regarding the propriety of their assessment of the data, whether they impermissibly analyzed a Level IV case series as Level II cohort data, whether and to what degree confounding factors or selection biases were present, whether they employed appropriate statistical analysis, and so on. See Transcript of Proceedings, Nov. 18, 2009, pp. 201-19, 223-28, 234-38. Given Dr. Greenland's testimony that the Hansen/Beck Study reflects a high association between continuous infusion and chondrolysis that is apparent through "common sense," the testimony and cross-examination of Drs. Greenland and Wells would likely confuse or mislead rather than assist the jury. Fed. R. Civ. P. 403.

To be clear, I do not find the lack of relevance or helpfulness a necessary byproduct of the methodologies employed by Drs. Greenland and Wells; rather, it results from the limits of the Hansen/Beck Study as presented to them. Regardless, while the methodologies employed by Drs. Greenland and Wells are reliable within the meaning of Rule 702 and *Daubert*, their testimony is not necessarily relevant and will not aid the jury's determination of causation. Should defendants "open the door" at trial such that the testimony of Drs. Greenland and Wells becomes relevant and helpful for purposes of rebuttal, I may reconsider the admission of their testimony.

#### E. Plaintiffs' Challenges to Defendants' Expert Witnesses

Plaintiffs similarly do not question the credentials or qualifications of defendants' experts. Instead, plaintiffs challenge the methodologies of two experts disclosed by defendants, Drs. Stetson

and Burkhead. Plaintiffs argue that their methodologies are unreliable, because they reviewed the medical literature in piecemeal fashion rather than in its totality and opine to unattainable levels of causation inconsistent with *Daubert's* flexible analytical framework.

#### 1. Dr. Stetson

Dr. William Stetson is an orthopedic surgeon from Burbank, California who has performed hundreds of shoulder arthroscopies, purportedly without observing a single case of chondrolysis. Dr. Stetson opines that the prevailing and generally accepted consensus in the orthopedic surgery community, as reflected by the peer-reviewed medical literature, is that the cause of chondrolysis is unknown and that factors other than continuous infusion must be considered as potential causes. Specifically, Dr. Stetson suggests that surgical error, such as the use of a glycine irrigant not normally used by surgeons, could be a causal factor in plaintiffs' development of chondrolysis.

Plaintiffs challenge two aspects of Dr. Stetson's opinion: that surgical error can be a contributing factor in the development of chondrolysis, and that he has performed approximately 500 arthroscopic procedures without one resulting case of chondrolysis. Plaintiffs emphasize that Dr. Stetson cites no studies on surgical error to support his opinion and cannot explain how surgical error could cause chondrolysis. Plaintiffs also emphasize that Dr. Stetson did not pursue follow-up examinations to detect chondrolysis in any of his patients.

I do not find Dr. Stetson's opinion unreliable on these grounds. Dr. Stetson does not state unequivocally that surgical error is an established cause of chondrolysis but only believes that it should be considered a factor when "clusters" of chondrolysis occur in the practice of a single surgeon. Dr. Stetson certainly may rely on his own clinical experience in stating his opinion, just as plaintiffs' experts are allowed to do.

## 2. Dr. Burkhead

Dr. Wayne Burkhead, Jr. is an orthopedic surgeon who practices in Dallas, Texas. Like Dr. Stetson, Dr. Burkhead has performed hundreds of shoulder surgeries including those with intra-articular placement of pain pumps for continuous infusion, with no reported cases of chondrolysis.

Plaintiffs first challenge Dr. Burkhead's testimony on grounds that he contacted pain pump manufacturers and offered his services as an expert witness. Burkhead Dep., Aug. 31, 2009, p. 17. However, plaintiffs point to no involvement or financial interest of Dr. Burkhead in, for example, the development of studies designed to disprove continuous infusion as a cause of chondrolysis. Absent evidence of actual bias - litigation or otherwise - I fail to discern why Dr. Burkhead's overture renders his opinion unreliable for purposes of *Daubert*.

Plaintiffs next challenge Dr. Burkhead's suggestion that surgical error and patients' ages contribute to the chondrolysis cases reported in the Hansen/Beck Study, and argue that Dr. Burkhead cannot rely on his own clinical experience because he performed no systematic review of his patients' records. However, Dr. Burkhead is entitled to draw inferences regarding causes of chondrolysis such as patient age and surgical error from the medical literature and his extensive experience. Plaintiffs' quibbles with Dr. Burkhead's opinion do not make his testimony unreliable and it will be admitted.

## CONCLUSION

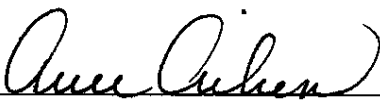
To fulfill its gate-keeping role, the court must strike "the appropriate balance between admitting reliable, helpful expert testimony and excluding misleading or confusing testimony." United States v. Rincon, 28 F.3d 921, 926 (9th Cir. 1994). *Daubert* counsels against rigid formulations of reliability and instead requires the court to carefully examine plaintiffs' experts' methodologies as applied to the specific facts presented, remaining mindful that plaintiffs' ultimate

burden is proof by a preponderance of the evidence. "Although this legal standard may lead to what some scientists might consider an unacceptably high error rate in jury verdicts, the law has tolerated the jury error rate for centuries because it has not yet found a better way of adjudicating disputes." In re Ephedra, 393 F. Supp. 2d at 193.

Applying these principles, I find the testimony of Dr. Matsen irreparably tainted by litigation bias and by counsel's involvement in the study underlying his opinion, and the testimony of Drs. Greenland and Wells, though based on reliable methodologies, ultimately unhelpful and potentially confusing to the jury. Pursuant to Rule 26, Dr. Basamania's testimony must exclude reference to his 2006 presentation, given the inability to produce relevant documents. Otherwise, I find the methodologies of plaintiffs' experts valid, reliable, and helpful, and their conclusions adequately supported by the evidence and knowledge upon which they rely.

Accordingly, defendants' Motions to Exclude Testimony of Plaintiffs' Experts as to General Causation are GRANTED with respect to Frederick Matsen, M.D., Sander Greenland, PhD, and Martin Wells, PhD., defendants' Renewed Motions to Strike the testimony of Dr. Matsen are GRANTED, and defendants' Motions to Strike the testimony of Dr. Basamania are GRANTED with respect to his 2006 presentation. Defendants' Motions to Exclude are DENIED in all other respects. Plaintiffs' Motions to Exclude Testimony of Defendants' General Causation Experts are DENIED. IT IS SO ORDERED.

DATED this 28 day of April, 2010.

  
 Ann Aiken  
 Chief United States District Judge